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THE PATHOGENESIS OF ATHEROSCLEROSIS.[1]

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"IN scarcely any other disease co-operate so many factors in its origin as in arteriosclerosis." So said Ludwig Aschoff in 1924—and I hope to be able to convince you of the truth of this aphorism.

I propose to deal mainly with the production of atherosclerosis in the experimental animal, leaving Dr. Hall to discuss the pathogenesis of the disease from the clinical side.

It is imperative that, at the outset, we try to get some order out of the chaos of nomenclature. You will note that the title of this symposium specifies "atherosclerosis", and this term will be used as synonymous with atheroma. I shall be quite dogmatic and state that it has an entirely different meaning from arteriosclerosis.

"Arteriosclerosis" is used extensively by the Americans, and frequently includes arterial degenerative changes in general. This usage has led to considerable confusion in the literature, especially in relation to experimental work. Often it is difficult to decide just what the authors do mean—whether they are talking about atherosclerosis or about some other condition associated with a more generalized and diffuse sclerosis of the arteries.

I take the term arteriosclerosis to mean a more or less generalized increase in fibrous connective tissue in the arterial wall, a change generally accompanying raised blood pressure. Much less commonly, arteriosclerosis is not associated with hypertension but is simply an aging process.

I am never quite sure what *clinicians mean when they* use the term arteriosclerosis—as, for instance, in the expression "arteriosclerotic cerebral vascular disease"; but I take it that included in such a blunderbuss diagnosis are many cases of atheroma of the cerebral vessels with its consequent *thrombosis, cerebral softening and such like.*

If during the course of this dissertation the name arterio*sclerosis is used, it is done with a purpose, for in much* experimental work the term is used by authors who do not make it quite clear what is actually being included under that title.

There have been many attempts to produce arterio*sclerosis, but none were successful until about fifty years* ago, when Josué in 1903 produced changes by repeated injections of adrenaline. However, these changes affected mainly the medial coat, and were not very closely allied to atherosclerosis, except that at a rather advanced stage *some intimal thickening occurred over the plaques, but no* lipoid appeared.

[1] Read at a meeting of the Section of Medicine and the Section of Pathology of the New South Wales Branch of the British Medical Association on July 12, 1955.

Experimental Cholesterol Atherosclerosis.

Definite lipoid deposits were finally successfully produced by Anitschkow and Chalatow in 1913, when they showed that feeding cholesterol to rabbits produced such deposits in the aortic intima, alleged to be morphologically similar to the naturally occurring disease in man. They described their findings in the following words:

> It resembles human athero-sclerosis very closely and therefore its more detailed investigation cannot but advance our knowledge of the pathogenesis and ætiology of that disease.

In spite of this, I am convinced that quite the contrary has happened. Clinicians and experimentalists have become so obsessed with the cholesterol hypothesis that most other approaches to the elucidation of the problem have been neglected. I am equally sure that the cholesterol side is practically worked out, and that any new major advance will come from a different angle.

There are good reasons for doubting the validity of drawing too close an analogy between the lesions induced in rabbits and the human disease. These reasons have been well summarized by Duff (1935), as follows:

1. Normally the rabbit's diet is very low in cholesterol, and massive doses have to be given and the blood cholesterol has to be raised to quite unphysiological levels; whereas in the human, generally speaking, there is no correlation between the extent of atheroma and the blood cholesterol levels.

2. The lesions in the rabbit are most advanced in the thoracic aorta, whereas the abdominal aorta is the site of election in the human. Similarly the cerebral vessels are never affected in the rabbit and renal vessels but seldom, in contradistinction to the human, in whom these arteries are frequently involved.

3. In the rabbit, the pulmonary artery is affected almost as much as the aorta—a state of affairs quite different from that found in the human, for in the latter the pulmonary artery is spared except in conditions associated with prolonged pulmonary hypertension.

4. Lastly, for the rabbit to develop cholesterol atherosclerosis, unless the cholesterol is given in small doses over very long periods, the body has to become more or less saturated with the substance, as shown by examination of the liver, lymphatic glands *et cetera*; but, generally speaking, no such state is to be found associated with atheroma in the human.

Similar objections can be raised against drawing too close a comparison between experimental cholesterol atherosclerosis in other animal species and in man.

The dog, for instance, develops lesions only after massive ingestion of cholesterol, and then only when the animal is submitted to thyroidectomy or to treatment with thiouracil (Steiner and Kendall, 1946). The blood cholesterol level has to rise about tenfold before lesions are produced, and when a positive result is finally achieved the main deposition of lipoid appears in the media in the first instance and not in the intima—a lesion which bears very little histological resemblance to the human disease.

Unfortunately, the majority of the smaller laboratory animals are resistant to most procedures aimed at the experimental production of atheroma; but Dauber and Katz (1942) have shown that the domestic fowl not only develops atheroma naturally, but can be provoked into doing so both by cholesterol feeding and by the exhibition of certain œstrogenic compounds. However, they point out that the cholesterol and stilbœstrol induced lesions differ from the naturally occurring ones. They state that the natural spontaneous lesion is fibrotic, while the induced lesions consist, in the early stages, of the intimal cushion of foam cells characteristic of most other forms of experimental atheroma.

I wonder how far we are justified in drawing any close analogy between chick and human atheroma—bearing in mind the fact that in the chick the natural and experimental lesions differ, and also not forgetting the great differences there must be in the physiology and feeding habits of the two species.

While we are considering the subject of experimental cholesterol atherosclerosis, it is opportune to draw your attention to the varying ideas about how cholesterol reaches the site and what part it takes in the formation of the atheromatous plaque.

1. The so-called imbibition theory was postulated by Virchow (1856) and supported by Aschoff. They thought that the first change was a certain loosening of the connective tissue ground substance of the intima, attributed in a large measure to an increased imbibition of fluid elements from the passing blood. When this thickening of the intima had advanced to a certain degree, fatty metamorphosis generally put in an appearance. They also believed that the primary cause of the loosening of the intimal coat was of a mechanical nature, the cholesterol only later being imbibed by the damaged tissue.

2. Perhaps as a corollary to the imbibition theory one might mention the work of Wilens (1951), who excised segments of iliac arteries and then filled the vessels with serum at varying pressures for a period of up to twenty-four hours. He found most of the cholesterol from the filtrate through the vessel wall to be deposited in the wall and concentrated in the intima, its further progress being stopped by the internal elastic lamina.

3. Leary (1941) did not agree with the imbibition theory. He believed that the cholesterol is first ingested by Küpfer cells in the liver and similar cells elsewhere; and when they are fully engorged, they become detached, are swept into the circulating blood and are carried to the arterial systems. These cells, by some chemotactic process, then pass through the endothelium and finally become trapped between this and the internal elastic lamina.

4. As another explanation of the pathogenesis of atherosclerosis, the theory of Winternitz (1938) and his colleagues might briefly be considered. They suggest that most of the changes are mediated by the *vasa vasorum*, which can be demonstrated in abundance in and around atheromatous plaques. According to this theory the lipoids and other constituents of the plaques are derived from exudation and hæmorrhage from the *vasa vasorum*.

Although this process may contribute to the disease in the older plaques, it can scarcely be regarded as effective in initiating the lesions, since vessels are rare in the intima of the normal human artery. Also, veins of the human which are highly vascularized are only rarely the seat of atherosclerosis.

5. A refinement of the cholesterol hypothesis has been elaborated by Gofman and his co-workers (1950). By means of the ultra-centrifuge they have subdivided the various lipoid-containing fractions in plasma and have classified them according to their flotation values—known as Svedberg Flotation Units or "Sf"—which vary between Sf2 and Sf40,000.

It is thought (Jones *et alii*, 1951) that the particles of the Sf 10 to 20 group are concerned in the pathogenesis of atherosclerosis, because this fraction appears in the serum of cholesterol-fed rabbits. Furthermore, the Sf 10 to 20 fraction is said to be statistically related to the atherogenesis in the human, although as Florey (1955) stated in his Halford oration recently: ". . . the position is by no means clear as the views seem to rest on statistical argument of somewhat doubtful validity."

6. A further refinement of the cholesterol hypothesis is claimed by differentiation between the importance of α and β lipoproteins. Now, cholesterol is mostly transported attached to different fractions of plasma protein and is kept in solution by phospholipids.

The proportion of α and β lipoproteins is related to age and sex. For instance, the amounts of β lipoproteins are found to be lower in women aged under forty-five years than in men, but are approximately the same in both sexes after that age. It is thought that these β lipoproteins contain the atherogenic fraction, and that this difference in ratio explains the sex distribution of coronary atheroma before the age of forty-five years.

7. The importance of cholesterol as a specific ætiological agent in the pathogenesis of atherosclerosis is, to my mind,

greatly diminished by the work of Hueper (1944), who demonstrated that other unrelated substances such as methyl-cellulose, polyvinyl alcohol and gum arabic cause similar intimal lesions. All of these macromolecular agents produce intimal accumulations of foam cells laden with the foreign material which are very similar to those seen with cholesterol. They are even followed by intimal proliferation and fibrosis. Hueper suggests that cholesterol and these other macromolecular compounds provoke intimal proliferation by causing anoxia of the underlying tissues. In other words, the cholesterol effect is non-specific.

Another point counting against the importance of cholesterol is that in experimental atherosclerosis, cholesterol does not take any great part in the formation of the very earliest lesion (McMillan, 1952). McMillan has shown that the lipoids participating in the initial formation of the plaque contain no demonstrable amounts of free cholesterol until several days after the lesion has begun to form. When cholesterol finally appears, it is not clear whether it is imbibed from the plasma or formed as a breakdown product *in situ* resulting from the metabolism of the foam cells.

In support of this experimental finding, it is possible to show that some of the smallest lesions in the human aorta are likewise free of demonstrable cholesterol.

I am in absolute agreement with Irvine H. Page (1954) when he said that "the time seems right for a change in the tactics of research to include mechanisms other than those directly concerned with lipoids".

Other Theories and Possible Lines of Pursuit.

The following are some other possible factors in the pathogenesis of atherogenesis: (i) effects of trauma on the vessel, (ii) hypertension, (iii) diabetes, (iv) mural encrustation theory of Duguid, (v) diet, (vi) heparin.

1. With trauma may be conveniently included the natural aging process.

For many years atherosclerosis was accepted as a normal and inevitable aging process and the attitude of "why attempt to prevent or cure the inevitable?" arose. Little imagination is required to appreciate the obstructive influence this senescent theory must have had on investigation. However, we must concede that age plays some part in the pathogenesis. The fact, I think, is accepted that usually atheroma is more common and much more advanced in the elderly; but we must not lose sight of the fact it is also found in quite young people. It is quite obvious that age is not the only factor, otherwise why should the aorta be so severely affected and yet the pulmonary artery generally spared?

Perhaps age is inseparable from trauma of one kind or another. In some parts of the arterial system mechanical stress and stretching of the walls of the vessels are more exaggerated than in others. For instance, the hydrostatic pressure is greater in the abdominal than in the thoracic aorta, in the systemic than in the pulmonary circulation; shearing strains are greater where branches are given off. If, with each heart beat, there occurs a minimal injury to these areas, there might well be a summation effect and, as time passes, so does the accumulated trauma gradually take effect, thus predisposing certain sites to the development of atherosclerosis.

There have been many experimental attempts to provoke the development of atherosclerosis by injuring vessels in one way or another, all producing either questionable or negative results. Local cauterization or freezing severely damages the media and produces some intimal proliferation, but any resemblance to atherosclerosis is quite remote. Other methods, such as stretching, bending and scratching, have also been unrewarding. Recently in my department attempts have been made to damage the rat's aorta by intense X-irradiation and by implantation of radon seeds. The X-ray treatment left the vessel unscathed, but it is too early yet to pass judgement on the efficacy of the radon. Surprisingly enough, the literature is absolutely void of any reference to the effects of irradiation on large blood vessels, and I am beginning to think that perhaps they are almost completely resistant.

In one experiment Wilens (1942) placed a silver collar around a rabbit's aorta prior to cholesterol feeding, and it was noted that atheroma always affected the part thus surrounded. Wilens concludes that the immobilization of the wall caused by the collar predisposes to the disease, and he compares this with the predilection shown by atheroma in the human aorta for sites of origin of branches—postulating that here, too, there is some fixation of the nearby aortic wall.

2. With regard to hypertension, in the human, simple observation indicates some correlation between hypertension and atherosclerosis, although this relationship is far from absolute, for many patients have advanced atheroma in the absence of hypertension, and *vice versa*.

Further facts seem to reinforce the conception that the two conditions are associated—for instance, the rarity of atheroma in the pulmonary arterial systems, except in cases of prolonged pulmonary hypertension occurring in such conditions as mitral stenosis and severe emphysema. Likewise it is generally agreed that atherosclerosis is usually well established in coarctation of the aorta in that part of the vessel proximal to the stenosis, whereas the distal portion is spared. Animal experiments have confirmed this, for as Dill and Isenhour (1942) have shown, if artificial coarctation is effected in rabbits, about one-third of the animals develop a considerable number of intimal plaques, many of which contain lipoid. These plaques are confined to the proximal portion of the aorta which is subject to the raised blood pressure, and are never seen distal to the constriction.

The hypertensive hypothesis may be closely linked with trauma, for it is reasonable to believe that with each systolic wave the stretching and shearing strains in the vessel walls of the hypertensive will be more severe, and therefore the cumulative trauma greater, than in the normotensive.

3. Although it is denied by a minority, "there can be little doubt", according to Warren and le Compte (1952), "that diabetics are prone to develop athero-sclerosis at an earlier age and to a greater extent than other persons". This observation has led to animal investigation along the same lines; but not only has experimental diabetes not led to the increased incidence of atheroma, but Duff and McMillan (1949) have shown that in rabbits, alloxan diabetes tends actually to inhibit cholesterol atherosclerosis.

Although many cases of diabetes in the human are associated with hypercholesterolæmia, this is not an invariable finding; also the degree of development of atheroma bears little correlation to the severity of the diabetes. To explain the increased incidence it has been suggested that as a result of fluctuations in the blood-sugar level there are rapid and substantial changes in the plasma osmotic pressure which cause swelling of the ground substance in the intima followed by lipoid infiltration, the latter being enhanced by any concomitant hypercholesterolæmia. It is clear how close this conception is to the imbibition theory of Virchow.

4. Next, we may profitably consider the newer conception of the pathogenesis of atherosclerosis of Duguid (1955), or rather the rediscovered or rejuvenated hypothesis of Rokitansky (1852). I think it is only fair to state at this juncture that I worked with Professor Duguid for a number of years, and so may show, not unnaturally, some slight bias in favour of his ideas. Rokitansky taught that atheroma was the product of mural thrombosis or, as he described it, "an excessive deposition of fibrin on the lining membrane of the vessels". This concept was rejected by the histologists of the day on the grounds that the lesions were in the vessel walls and not on them. They failed to recognize that when fibrin is deposited on the intima it very quickly becomes covered with endothelium so that it is incorporated in the vessel wall, and that any further changes that occur in the fibrin appear as if they were in the vessel wall itself rather than on the surface.

This theory postulates that partial organization of the fibrin occurs, and the remainder of the clot so changes its appearance that it might easily be mistaken for some kind of degeneration of the intimal tissues. Finally fatty changes make their appearance in the thrombi, and the condition is then identified as atherosclerosis. The fatty change is first noted as a fine sprinkling of lipid droplets amongst the thrombotic elements, and they soon become the most prominent feature. Softening may later occur so that typical atheromatous material is formed.

Support for this theory is found, not only in observation of human material, but also in experimental evidence by various workers who have injected fibrin clot intravascularly and have been able to demonstrate its incorporation into the vessel wall as Rokitansky suggested.

Duguid has expanded the idea of mural deposits by repeating the cholesterol feeding experiments on rabbits and studying the earliest changes. Rannie and he (1953) have shown that the lipoid-laden phagocytes do not, in fact, invade the intima, but lie on its surface in repeated layers, the oldest layer nearest the intima becoming fibrous, and the whole covered by endothelium to give the misleading appearance of lipoid accumulation within the original vessel wall.

It is suggested, then, that atherosclerosis may arise by two different processes—by mural thrombosis on the one hand and by deposition of lipid-bearing cells on the other. It is obvious that in both processes the mechanism is the same in so far as the arteries are concerned; solid matter is deposited on the intimal surface and in due course covered by endothelium, so becoming incorporated in the intima. It is quite likely that the superficial fatty streaking seen in the aortas of young people is the result of such mural lipoid deposits, and perhaps these lesions, appearing early in life, predispose to fibrin deposition and thus to the formation of true atherosclerosis later on.

At this stage it is as well to mention that there are a group of substances known as fibrinolysins in the circulating blood, and that these vary in amount from time to time and in association with disease. If the level drops, it is quite possible that deposition of fibrin is accelerated, and so conceivable that the level of circulating fibrinolysins controls to some extent the rate of development of atheroma.

5. What is the relationship in the human, if any, between diet and the occurrence of atheroma? Diet may possibly affect the development of atherosclerosis in two ways, both being involved with lipoid metabolism. Firstly, as has just been mentioned, lipoid may cause the juvenile form of atheroma and thus predispose to mural thrombosis. Secondly, diet may affect the coagulability of the blood, for it has been shown that alimentary lipæmia following a fatty meal is accompanied by an accelerated clotting time, and it is as well to remember that certain factors of a lipoid nature are concerned in blood coagulation. By these means an excessively fatty diet may predispose to mural thrombosis and so to atheroma. This may account for the apparent relationship between obesity and the severity of atheroma.

6. Lastly, the part played by heparin and heparin-like substances in the pathogenesis of atherosclerosis must be considered. In 1943 Hahn observed that an injection of heparin caused the clearing of lipæmic dog's plasma, apparently so changing the structure of the chylomicrons as to make them water-soluble. Ten years later Constantinides *et alii* (1953) showed that heparin administered to cholesterol-fed rabbits prevented lipæmia, reduced hypercholesterolæmia and greatly retarded the development of experimental atherosclerosis.

It is not obvious how this finding in experimental animals can help in the interpretation of the pathogenesis of the disease in man. Is it going too far to suggest that the plasma clearing action is incidental, and that heparin retards the development of atherosclerosis simply by diminishing the extent of mural clot formation (of the Duguid hypothesis)?

Conclusion.

It is now clear, I hope, that the problem of the pathogenesis of atherosclerosis remains far from solved. Some of the outstanding questions are: What is the original lesion in the vessel wall? Does cholesterol initiate the process, or is it only a relatively late participant? How do hypertension and diabetes aggravate the disease? What part does mural thrombosis play? Obviously there is no simple answer—many factors must be involved, and I will end with another quotation, this time from Duff and McMillan (1951):

> The clear recognition and understanding of all the factors concerned in the ætiology and pathogenesis of athero-sclerosis must await the future.

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A CLINICIAN'S VIEWS ON THE PATHOGENESIS OF ATHEROSCLEROSIS.[1]

By GEORGE V. HALL,
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It is always with trepidation that I approach the subject of atherosclerosis—firstly, because I feel that I can contribute so little to it, and secondly, because I feel that in some circles it is regarded as a hardly respectable subject for a clinician. I take comfort in the fact that knowledge of the nature of atherosclerosis, generally speaking, is primitive anyhow. I also hope that a brief statement of the problem from the clinician's viewpoint may stimulate discussion and investigation, which is preferable to the apathetic acceptance of atherosclerosis as an inevitable consequence of aging.

This latter view was expressed by Boyd (1943), when he wrote: "Atherosclerosis is a degenerative process usually associated with advancing years which in one way seems as natural as the greying of the hair. It is the end of a song which is sung in the cradle." The other extreme is represented by the over-enthusiastic medicine man with his superstitions based upon reproduction of the condition with uncertain fidelity in experimental animals under highly abnormal conditions. As a result of this misplaced enthusiasm, unfortunate patients have been subjected to iodism, starvation or intolerable diets with little justification.

As a basis for discussion I will make a brief statement now on each of thirteen points which most interested me in relation to this subject.

1. Atherosclerosis is by far the greatest cause of morbidity and mortality in the civilized world of today.

2. What knowledge we have of its pathogenesis is almost entirely theoretical. We have no methods for its detection clinically, and there is no treatment.

3. The disease is associated with aging. It develops much more rapidly in some individuals than in others. It may be the end of a song that is sung in the cradle, but the song reaches its climax in some people much earlier than it does in others.

4. Heredity plays a vital role in its development.

5. The condition tends to develop earlier in males than in females.

6. Arterial hypertension predisposes to the development of the condition.

7. Arterial anatomy predisposing to high lateral pressure seems to predispose to the development of the condition.

8. Endocrine glands, including the thyroid, the pancreas and the gonads, may play a part in the pathogenesis.

9. Heparin-like substances in the plasma may be an important influence.

10. Thrombogenesis and the labile nature of the arterial intima may play an important role in pathogenesis (Duguid).

11. In countries and communities where the average diet is characterized by high lipoid intake there appears to be a high incidence of the disease.

12. Hyperlipæmia and conditions of the suspension of the plasma lipoids and protein may play a part in the pathogenesis.

13. *Diabetes mellitus* predisposes to the premature development of atherosclerosis.

Perhaps we may now briefly discuss each point separately.

Morbidity and Mortality of Atherosclerosis.

It seems indisputable that atherosclerosis is by far the greatest single cause of morbidity and mortality in the western world of today. It manifests itself clinically in the guise of coronary disease, cerebral vascular disease and peripheral vascular disease. With the control of infections, and to a lesser extent of metabolic diseases, more people are undoubtedly living to the atheroma age group. But when allowance is made for this, the increase seems to be a real one, and the disease is an ever-increasing menace to men in the middle decades of life.

It is interesting that Ruffier (1922) found that the old Egyptians suffered from arterial lesions identical with those prevalent today. It is also interesting to note that the Egyptians did not smoke, nor were they inclined to be drunkards. Meat was a luxury in their diet, and they no doubt had their burdens and stresses comparable with those of today, such as plague, the building of pyramids, the Ethiopian expeditions, and the taxes imposed to pay for them.

Knowledge of the Pathogenesis of Atherosclerosis.

Passing on to the second point, we may say that our knowledge of the ætiology of the condition is comparable with that of the Egyptians three thousand years ago. They probably had almost as little insight into its ætiology as we have, but probably fewer theories like those which have plagued us over the past fifty years. To date there are no practical or reliable methods for the detection of atherosclerosis clinically, and there is no treatment.

The Association of Atherosclerosis with Aging.

In discussion of the third point we may say that, all things being equal, age has a direct bearing upon both the incidence and the intensity of atherosclerosis. If atherosclerosis is absent at birth, it becomes grossly visible approximately in late adolescence and becomes more widespread and more intense in the declining years. This applies not only to man, but to animals whose life tenure is not too short. However, atherosclerosis develops much more rapidly in some individuals than in others. Yater and his co-workers (1948) reported 866 cases of coronary artery disease in men of the American army aged from eighteen to thirty-nine years; 203 of these were under the age of thirty years. In all fatal cases there was extensive atheroma of the coronary vessels. Adlersberg (1952) compared a group of 50 persons below the age of forty-six years who died of coronary artery occlusion with another group of 50 who were aged sixty years or over and had died from the same cause. The microscopic appearance of the coronary arteries was indistinguishable in the two groups. From what evidence we have it seems that between the periods of weaning and adolescence atherosclerosis is a reversible process. After this the rate and deposition of lipoid are influenced by various factors. There is grave doubt whether it becomes completely reversible. Why the condition develops to its full extent in some individuals so much earlier than in others is unknown. It may be something to do with the constitution of the plasma which bathes the arterial intima or it may be due to changes in the vessel walls, especially the ground substance. In these respects heredity appears to play an important part.

Heredity and Atherosclerosis.

It has been recognized for many years that atherosclerosis, particularly involving coronary arteries, runs in families. A single dominant gene may be involved, but as Glass (1953) has pointed out, genes rarely produce absolute effects, but determine an individual's capacities and the nature of his reactions under specific conditions. Beas and Adlersberg (1945) reported that patients with coronary atherosclerosis exhibit a pattern not unlike that in families with xanthoma. Alvord reported that 15 members of one family had hyperlipæmia, six had *xanthoma tuberosum* and 18 a history suggesting disease of the coronary arteries. They all seemed predisposed to atherosclerosis. Sprague (1950) and his co-workers suggest that an individual with predominant muscularity compactness and maleness, the so-called mesomorphic type, is most likely to have a myocardial infarct under the age of forty years.

[1] Read at a meeting of the Section of Medicine and the Section of Pathology of the New South Wales Branch of the British Medical Association on July 12, 1955.

Sex Incidence of Atherosclerosis.

Atherosclerosis has been considered by various authorities as much as seven times as common in men as in women. This observation has, of course, led to the investigation of the gonadal hormones and their relation to possible ætiological factors. It has been recorded that in women who have undergone bilateral oophorectomy the incidence and extent of atheroma are greater than in the control group. This has led to the suggestion that œstrogens may be of value in the prevention of atherosclerosis in people disposed to this condition. We have this matter at present under investigation at Saint Vincent's Hospital.

Hypertension and Atherosclerosis.

The effects of hypertension in the development of atherosclerosis are perhaps best understood by a study of the greater and pulmonary circulations. As has been pointed out by Professor Magarey, gross atherosclerosis affecting both the aorta and the pulmonary arteries simultaneously is the exception rather than the rule. Since there is no reason to suspect a difference in tissue susceptibility between the systemic and the pulmonary vasculature, the difference in incidence of atherosclerosis between the systemic circulation and the pulmonary circulation is deeply significant, since it excludes any toxic, metabolic or infectious factors, as the same blood bathes both parts of the circulation.

Under what circumstances does atherosclerosis in the pulmonary circulation arise? It occurs in emphysema, in mitral disease, in obliterative lesions of the lung, in prolonged congestive cardiac failure, and in open shunts between the two sides of the heart when the shunt is from left to right. A common factor in all these conditions is an increase in the pressure in the pulmonary artery. There seems no doubt that the normal blood pressure is an important causative factor in atherosclerosis, since its incidence is lower in hypotensive diseases. When hypertension supervenes, the age limit for the production of atherosclerosis is lowered and the lesions are intensified. Normotensive young and middle-aged women are far less likely to develop myocardial ischæmia and infarction than men of the corresponding age groups. When hypertension develops in women of these age groups, the incidence of coronary atherosclerosis approaches that in the male. Hypertension accounts for practically all the cases of juvenile atherosclerosis, with the exception of diabetic subjects.

Arterial Anatomy and Atherosclerosis.

Atherosclerosis is not uniformly distributed throughout the arteries in the body. The regions predominantly involved are those subjected to the greatest intravascular pressure. Arterial blood pressure has two components: a static or lateral head and a velocity head. When the blood flow is obstructed the velocity head is converted to the static lateral head which is exerted against the arterial wall. This is perhaps the reason for the apparent predilection to atheroma of the anterior descending branch of the left coronary artery. During ventricular systole there is considerable retardation of systolic flow, owing to the high level of intramural systolic pressure in the left ventricle. Also atheromatous lesions are prominent at points such as the bifurcation of the aorta, and the sites of origin of intercostal and lumbar arteries, where the blood flow is to an extent obstructed.

The incidence and location of atherosclerotic patches are conditioned not only by the intraarterial pressure, but also by the external resistance. This may be why the arteries of the mesentery are notably free from gross atherosclerosis, since they are mostly surrounded by the gas-containing gut. In contrast to the arteries, the veins, even in the aged, are usually free from atheroma. This is because the pressure in the veins hovers around zero, and when venous pressure rises, as for instance in congestive cardiac failure or constrictive pericarditis, it never even approximates the normal systolic blood pressure.

The Role of the Endocrines in Atherosclerosis.

Experimental investigation of the role of the endocrines in atherosclerosis has been centred around the thyroid, pancreas and gonads. Atherosclerosis is shown to be more prominent in both men and animals when they are in a hypothyroid state. The development of the disease appears to be accelerated in patients with myxœdema. Experimentally the disease can be produced in the dog by cholesterol and lipoid feeding only after the basal metabolic rate has been lowered by the administration of antithyroid drugs.

Thyroid may act in controlling the intensity of hyperlipæmia, and it may also act by its action on the arterial intima. There is some evidence that permeability of the intima is decreased by thyroid hormone. The action of thyroid hormone in relation to this disease appears to be a complex problem. Pancreatic secretion has long been associated with atherosclerosis. It has been postulated by Dragstedt that there is an internal secretion of the pancreas, which he calls lipocaic, which plays a role in fat metabolism analogous to that of insulin in carbohydrate metabolism. This, however, remains to be proved.

The increased incidence of coronary artery disease in the male has been remarked upon, and the possible role of œstrogens has been mentioned. The effect of œstrogens on the plasma lipoids has been studied, and it has been stated that those lipoid particles most likely to be deposited in the arterial intima rise slowly in concentration in the plasma of females between puberty and the menopause, in contrast to the sharp rise near the twenty-fifth year in the male. Both sexes are equal beyond the age of sixty years.

Heparin and Atherosclerosis.

The effects of heparin in clearing the lipæmic plasma of experimental animals has already been discussed by Professor Magarey. Block, Mann and Barker (1950) showed that intravenous doses of three milligrammes of heparin differentiated normal plasma from atherosclerotic plasma three hours after a fatty meal, as atherosclerotic plasma cleared less rapidly.

Depression of large lipoid particles with flotation rates Sf 12 to 20 was noted in both normal adults and myocardial infarction patients after the administration of 50 to 100 milligrammes of heparin intravenously at intervals of three days. When medication was discontinued, pretreatment level was reestablished in a month. Graham and his co-workers went on to show that 55 of 59 patients under prolonged heparin medication were strikingly relieved of their angina, and they claimed that this effect was brought about by the action of heparin in clearing the plasma of blood lipoids. The lipoid-clearing effect is counteracted by the administration of protamine.

In my own experience I have been impressed by the rapid relief of pain following myocardial infarction in some patients. Other patients do not get this prompt relief. The relief in some is so prompt and dramatic that one feels that the most likely explanation is a vasodilatory effect rather than a plasma-clearing or pure anticoagulant action.

From my own experience I have also been impressed by the lessening of the frequency and severity of anginal pain by intravenous injection of heparin in some people with myocardial ischæmia due to coronary insufficiency. This coincides with Graham's experience mentioned above, but his explanation of a plasma-clearing effect in relation to blood lipoids is open to doubt. I am intrigued by the fact that the relief is obtained in some with intravenous injections given at relatively long intervals, even forty-eight to seventy-two hours apart. Perhaps the most likely explanation for this action is an anticoagulant effect. Professor Magarey has pointed out that hyperlipæmia tends to increase the liability to clotting, and in this way the plasma-clearing action and the anticoagulant effect may be linked.

The rapid relief of anginal pain by the intravenous injection of heparin may be due to the inactivation of a

vasoconstrictor substance called serotonin. This substance, which is produced at the site of intravascular clotting, has been isolated and synthesized and its vasoconstrictor action has been proved. It has also been demonstrated that it is inactivated by heparin.

I am indebted to Dr. F. Byrom for this information.

Thrombogenesis and the Labile Nature of the Arterial Intima.

Professor Duguid's theory of thrombogenesis has been admirably explained by Professor Magarey. Professor Magarey has worked with Professor Duguid in this very important field, and so I will not presume to paint refined gold or gild the lily. I feel that further investigation along these lines is more likely to bear fruit in the unravelling of the mystery of the pathogenesis of atherosclerosis than the following of some of the current more popular theories.

No one seriously believes that atheroma is commonly developed by episodes of relatively gross thrombosis. In human pathology it would appear that the role of thrombogenesis must stand or fall with the question of microscopic coagula and fibrinous encrustations, and with further inquiry into the application of the work to the collateral circulation. Duguid (1954) envisages that the blood in the circulation is not perfectly fluid and that the endothelium is not perfectly non-wettable. With the increasing imperfections of age, increasing deposits from the circulating blood upon the vascular endothelium are to be expected, and hence there is an increasing build-up of intimal thickenings by slow assimilation and organization of the deposits. There is the view that: "It is not so much that a man is as old as his arteries, but that he is as young as the adventitious vasculature in the walls of his arteries. That is to say, fibrinous encrustations may vary ultimately in their disposal according to the efficiency of mural vascularization."

Diet and Atherosclerosis.

Since the feeding of large amounts of cholesterol results in experimental atherosclerosis in some animal species, and some of the cholesterol fed is found actualiy in the atherosclerotic plaques, dietary cholesterol has long been suspect as a chief offender in the development of atherosclerosis.

Statistical evidence has been provided that populations consuming diets of low fat and low caloric contents have low serum cholesterol values, and that these do not increase with age. Where the diets are high in fats and calories, as in America, England and Denmark, serum cholesterol levels considerably exceed those in such low-fat diet countries as Italy, Spain and parts of Africa.

Most investigators hold that it is the amount of fat rather than the cholesterol consumed which is crucial in the effect of diet on serum cholesterol content. This is in contrast to the results of fat and cholesterol feeding in animals. It has been known for many years that cholesterol feeding in man produces little or no change in plasma cholesterol content. The feeding of fats, however, whether vegetable or animal, does seem to influence this level. There appears to be remarkable variety in the responses to diet. Some persons are highly sensitive to dietary lipoid changes, whilst others are not. This fact has led to attempts being made to evolve a type of lipoid tolerance test. No practical method has yet been evolved. The relationship of the development of atherosclerosis to obesity is not altogether clear.

Some authorities hold that obesity favours the development of atherosclerosis only when it is associated with hypertension. However, I believe that most clinicians will agree with me when I say that from my own experience the incidence of cardio-vascular disease is higher in obese patients than in others. Insurance companies have produced actuarial statistics to support this contention.

Lipoid Metabolism and Atherosclerosis.

The claims of the supporters of the hyperlipæmic and the disordered lipoid metabolism theory in the pathogenesis of atherosclerosis may be summarized as follows.

The Deposition of Lipoid Material.

The primary lesion of atheroma is held to be the deposition of lipoid material, mainly cholesterol ester, in the deepest part of the intima. The possible factors influencing the deposition of cholesterol in the arterial subintima are listed as follows: (i) the degree of hyperlipæmia; (ii) the physical state of the lipoid colloids; (iii) the colloid suspension state in the plasma; (iv) the intravascular filtration pressure; (v) the permeability of the arterial intima; (vi) the efficiency of the mechanism for removing deposited cholesterol from the arterial wall.

The other factors which may influence the deposition of lipoid material in the arterial intima have already been adequately discussed by Professor Magarey. The physical state of the lipoid colloids and the colloid suspension state in the plasma are regarded as points of particular importance by the protagonists of the lipoid metabolism theory.

The Hyperlipæmic Factor.

The evidence in favour of the hyperlipæmic factor may be summarized as follows.

1. Diet. (i) The experimental production of atherosclerosis in the rabbit, guinea-pig, chick and dog by sustained dietary elevation of blood cholesterol. (ii) The higher incidence of atheroma in people on a high cholesterol diet compared with the incidence of atheroma in people on a low cholesterol diet—for example, high-caste Chinese and Americans (particularly American army) compared with the low-caste Chinese and other Eastern people. Recently doubt has been cast on the validity of this comparison by Gertler *et alii* (1950).

2. Serum lipoid levels in people with overt atherosclerosis. Higher total serum cholesterol in coronary heart disease (maximal difference in serum cholesterol esters) has been demonstrated by Gertler *et alii* (1950) and by Turner and Steiner *et alii* (1939).

3. High incidence of atheroma in metabolic diseases associated with high serum cholesterol levels. This has been shown in essential xanthomatosis and other lipoidoses, "cholesterol families", *diabetes mellitus*, myxœdema, Ellis type II (or "nephrotic") nephritis, starvation.

It is important to remember that this work should be kept in true perspective when the problem of atherosclerosis is being considered as a whole.

We should not be carried away by the attractive implications of a theory largely based on statistical evidence, which can be very deceptive.

The Relationship of Diabetes Mellitus to Atherosclerosis.

I agree with the views expressed by Professor Magarey on the relation of *diabetes mellitus* to the development of atherosclerosis.

In these days, when we rely on insulin and diets of relatively low lipoid content for the control of the disease, it is rare to see patients with *diabetes mellitus* with prolonged hypercholesterolæmia or hyperlipæmia. However, diabetic patients, particularly the younger ones, still prematurely develop clinical manifestations of arterial degeneration. Even when control by our present clinical standards is strict, this is too often a tragic reality. Surely this must mean that there is a factor other than hyperlipæmia which leads to arterial degeneration in diabetes, and this other factor is probably more important than the hyperlipæmic factor.

However, we should not relax our strict control of the young severely diabetic patient, because the maintenance of a normal blood sugar content and the avoidance of hyperlipæmia certainly lower the incidence of premature arterial degeneration, even if they do not prevent it.

This concludes my remarks on the thirteen points which we have considered as having some bearing on the pathogenesis of atherosclerosis.

The Management of Atherosclerosis.

Have we gained any information which may be of practical value in the management of patients with atherosclerosis? There is very little of real value, I am afraid.

Detection of Latent Atherosclerosis.

In the first place, is there any way of detecting latent atherosclerosis? No problem in the field needs an answer more urgently, but we have none. We can only suspect that individuals may be susceptible from the family history and possible stigmata, such as premature aging in appearance or xanthomatous manifestations, such as xanthelasma taken in conjunction with the family history. There are no practical laboratory methods to assist us in the detection of latent cases. High serum cholesterol and serum lipoid levels in people with xanthomatous lesions or with very strong family histories may be some indication.

Treatment of Atherosclerosis.

There is no known treatment of value. There has been recently an influx on the drug market of a variety of mixtures of lipotrophic substances, of vitamins, minerals and amino acids, but none of them are of proved value and few have any semblance of experimental evidence to support their use. To use them is only to contribute to logical delinquency in the mind of the prescribing physician. It represents mechanized medicine at its worst.

Are we to give any advice, then, to patients who appear to be susceptible to the disease or who already have manifestations? Perhaps it would be reasonable to suggest dietary restrictions in certain classes of individuals. It would perhaps be wise for overweight subjects, particularly if they have a bad family history for vascular disease, to restrict their calorie and fat intake. Perhaps the same restrictions could be suggested for patients who are not overweight, but who have a bad family history with regard to vascular accidents, and who in addition have a raised serum cholesterol level or hyperlipæmia. To patients with overt atherosclerosis of the coronary vessels, aorta and coronary vessels, the same dietary principles could be suggested. Dietary restrictions should not be too severe. If there is severe restriction of fat intake, it may produce a feeling of depression and irritability and gastro-intestinal disturbances. Perhaps a lipoid intake of approximately half the normal level would be a reasonable restriction. The reaction of individuals will vary, and if the diet interferes too much with the patient's well-being it should not be persisted with.

In cases in which there is a high serum cholesterol level or hyperlipæmia small doses of thyroid could justifiably be given and maintained if there is no contraindication. I do not believe that any other so-called lipotrophic substances are worth using in our present state of knowledge.

We must strive at all times, of course, to control arterial hypertension and *diabetes mellitus* adequately, particularly in the young.

We know that these factors, if uncontrolled, will lead to the premature development of atherosclerosis as well as to other types of arterial degeneration. By the latter I refer to such conditions as the arteriolonecrosis of malignant hypertension and the hyaloid degeneration of the Kimmelstiel-Wilson syndrome.

What we mean by the strict control of *diabetes mellitus* and arterial hypertension is another story. I would just mention that we should always strive to maintain a normal blood sugar level in the young diabetic. We should also remember that a diastolic blood pressure of 130 millimetres or more will soon be followed by clinical manifestations of arterial degeneration in the young or middle-aged, if it is left uncontrolled.

Let us hope that as our knowledge of the pathogenesis of atherosclerosis increases, more attractive and practical methods of treatment will be evolved than starvation, medical castration and parent selection.

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A FURTHER STUDY OF RURAL FŒTAL MORTALITY.

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IN 1953 a report on an investigation of a country midwifery practice with the preliminary results in 300 cases following improved obstetrical care was published in this journal (Cullen, 1953). Further results reported in this paper confirm those preliminary findings.

In a total of 515 cases the combined mortality under one year was 14 deaths. The expected number of deaths, the Western Australian country average for the years 1948 to 1953 being used as a basis, is 23·7. The deviation from expectation is significant at the 5% level; that is, the improvement over the Western Australian country figures has been a significant one.

There were a further three deaths in 25 deliveries among unbooked patients, including holiday-makers and neighbouring town patients sent to this hospital in an emergency.

The total sample of 348 families was studied to determine differences in the social and economic status of the country town and farm groups, as this practice is considered to be in a typical Western Australian dairying population. The town of Busselton, which serves a population of 5500, lies on the coast 150 miles from the nearest city (Perth) with major consultant facilities. The journey to Perth takes three hours for an ambulance patient. The hospital has about 50 beds, of which 10 are for midwifery cases. The patients were divided into two main groups, the town and the farming.

The inquiry has been widened since the preliminary report to include all deaths under the age of one year. Five of the infants who died (0·9%) had congenital abnormalities incompatible with life, this incidence corresponding with recent Scottish experience (Record and McKeown, 1949), in which approximately 1% of all infants born died of a congenital malformation in the first year of life. One child was found dead in bed from staphylococcal septicæmia. The remaining 11 deaths could possibly have been prevented with better social conditions or medical management.

The most recent statistics reveal a continued difference in the metropolitan and country mortality rates, but this is due mainly to the differences in neonatal death rates

TABLE I.

Australia: Vital Statistics. Infant Mortality Rates, Metropolitan and Others, per Thousand Live Births.

Year.	New South Wales.			Victoria.			Queensland.			South Australia.			Western Australia.			Tasmania.			Australia.	
	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other. (a)	Whole.
1947	26·82	32·36	—	26·82	25·57	—	34·59	28·70	—	20·73	28·91	—	26·99	35·18	—	31·52	25·21	—	27·21	29·73	(b)
1952	20·71	26·96	24·5	21·69	22·96	22·2	23·73	25·60	24·9	21·29	25·31	23·0	23·52	26·27	24·9	21·62	21·77	21·7	21·73	25·38	23·79
1953	21·54	26·66	24·6	19·56	22·88	21·5	21·02	27·14	24·0	19·71	21·79	20·6	23·28	24·36	24·8	22·16	23·18	22·9	20·78	25·23	23·30
1954	(b)	(b)	25·2	18·61	20·21	19·3	(b)	(b)	22·3	(b)	(b)	21·2	(b)	(b)	22·5	(b)	(b)	23·9	(b)	(b)	22·46

TABLE II.

Australia: Vital Statistics. Stillbirth Rates per Thousand Total Births.

Year.	New South Wales.			Victoria.			Queensland.			South Australia.			Western Australia.			Tasmania.			Australia. (c). Total.
	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	Metropolitan.	Other.	Whole.	
1947	18·63	21·74	20·09	(b)	(b)	19·68	(b)	(b)	22·98	(b)	(b)	23·17	22·74	23·43	23·07	24·80	25·82	25·52	21·31
1952	14·53	16·71	15·85	(b)	(b)	16·81	(b)	(b)	18·89	(b)	(b)	17·58	16·16	19·97	18·03	15·33	20·63	19·08	17·01
1953	15·33	17·25	16·51	(b)	(b)	16·51	(b)	(b)	18·65	(b)	(b)	15·56	17·16	16·10	16·62	16·07	18·42	17·90	16·82
1954	(b)	(b)	16·24	(b)	(b)	14·46	(b)	(b)	17·46	(b)	(b)	13·82	(b)	(b)	16·67	15·40	15·78	(b)	(b)

(a) Includes Northern Territory and Australian Capital Territory.
(b) Not available.

rather than the stillbirth rates. Table I, giving the Australian figures for the period from 1947 to 1953, shows the fall in the metropolitan deaths under the age of one year to be from 27·21 to 20·78 per 1000 live births, and the fall in the corresponding country deaths from 29·73 to 25·23 per 1000 live births.

Stillbirth rates in those States in which metropolitan and country figures are separated are fairly close; Tasmania and Western Australia have a better country rate in their latest figures, and New South Wales has a persistently favourable metropolitan rate.

In view of this information, particular attention has been paid to further inquiries into the following: (i) the causes of the preventible deaths; (ii) the weaknesses in neonatal and post-natal management, and their possible correction; (iii) the important help given by the consultant; (iv) present trends in the management of labour and antepartum hæmorrhage; (v) why certain procedures have been found impracticable; (vi) better control of infections by the creation of a small laboratory; (vii) the current influence of social conditions upon fœtal mortality.

The Preventible Deaths.

Six deaths (five congenital and one due to staphylococcal septicæmia) were not preventible. The remaining six predominantly obstetrical deaths, and five pædiatric deaths, were theoretically at least capable of being avoided by more vigorous intervention on someone's part.

Three deaths resulted from difficult confinements (precipitate labour, obstructed labour and first-stage fœtal distress); more careful and experienced assessment by both staff and doctor might have saved the infants. One would expect this group to be very much larger. It is surprising how few patients have had unsuccessful terminations to their pregnancies purely on account of too conservative management (3 in 540). Two deaths (from preeclamptic toxæmia and accidental hæmorrhage) were due to lax instructions to the patients. The Women's Hospital, Crown Street, Sydney, first proved that extraordinary thoroughness in the prevention of toxæmia pays handsome dividends and is something upon which we can all insist in our own practice. The amount of trouble to which *primiparæ* particularly will submit in their interests, if the need is pointed out to them, is a constant reminder that we have only to direct them, and the majority will gladly carry out instructions.

A further three deaths (from pneumonia, gastro-enteritis and intraperitoneal hæmorrhage) might have been prevented if I had realized the critical nature of the illness in time to accelerate treatment. Looking backwards, one cannot help being appalled at the indifference with which one regarded such obviously serious symptoms as extreme pallor, cyanosis and dyspnœa in all three babies.

The remaining three deaths were directly sociological, and could be prevented only by combined economic, medical and educational instruction (chronic nephritis in a *multipara* and an accident to a farm-working wife).

Accidents to pregnant women are common, and I regret that an exact record of all falls or injuries has not been kept. However, three patients received direct abdominal injuries contributing to the fœtal death, and another two had work that was mechanically too heavy. Two other patients were brought into labour prematurely by falls, but came to no harm. In the past, accidents have been an insignificant cause of fœtal deaths, but with lower mortality they will have increasing importance (compare Clements, 1955).

A notable omission from the causes of death was poor nursing. This was unexpected. Since 1948 partly trained staff, lack of staff, or inability to keep off duty obvious carriers of staphylococci have been frequent and worrying, but no death has been due to bad nursing. Unnecessary morbidity has certainly been due to staff difficulties, and undue worry to the medical attendant has been frequent. It would appear reasonable that the onus of total and final responsibility should in every case be on the medical attendant, and that better results will be achieved if we

accept this rule—not to blame unsatisfactory staff, but to learn to anticipate trouble when untrained staff are in attendance.

Neonatal and Post-Neonatal Paediatrics.

Obstetrics is to many practitioners a very satisfying type of work, in which experience gives increasing confidence and probably better results. To many, including myself, pædiatrics—and particularly the neonatal cases—present a more difficult problem which has been partly created by too little post-graduate instruction. This has resulted at various times in the following mistakes: lack of appreciation of what constitutes an emergency; poor examination technique, or insufficient daily examination of the sick infant; poor cross-infection measures, and ignorance of what can be done to save some of the babies suffering from rare conditions who have previously been lost. On two occasions obstetricians instead of pædiatricians were telephoned about neonatal problems; some of the obstetricians have also not been through the hard school of the modern revolution in child health. The following cases illustrate these errors. One case of empyema was diagnosed five days late. A case of supraventricular tachycardia was missed. A diaphragmatic hernia remained undiagnosed because the possibility was not considered. Babies with gastro-enteritis and pneumonia died only a day or so after they had been considered to be not very ill. A case of *Bacterium coli* meningitis was undetected because pyrexia and vomiting were ignored. Rapidity of change in infants was not appreciated, and an intraperitoneal hæmorrhage in an hæmorrhagic diathesis was fatal before effective treatment could perhaps have been instituted. In case the general practitioners reading this analysis think it a little severe, my answer lies in the results now being obtained in any major pædiatric unit.

The following measures have been carried out in an attempt to improve this state of affairs.

1. Any baby reported by the staff as sick must be examined by the medical attendant; a telephone report will not do.

2. A cyanosed baby is considered to present an extreme emergency demanding one's immediate presence in the nursery. It is of interest that seven out of 18 babies reported as cyanosed in the nursery (not including the labour ward) died from varying causes.

3. When any baby was ill, a telephone consultation was held with a consultant pædiatrician.

4. If the condition of the child showed no improvement in a reasonable time, he was immediately transferred by ambulance to Perth.

5. Hand-washing, the use of masks, authority to enter the nursery and instructions to the staff to report the infant's minor symptoms, have all been encouraged with the assistance of the matron.

6. Regular attendance at the Princess Margaret Hospital for post-graduate instruction and ward rounds has been instituted. This is comparatively easy to do, as most hospitals that I have visited welcome practitioners joining ward rounds.

Have these measures had any visible results? The answer lies in a more aggressive attitude to neonatal difficulties. Neonatal infections are being treated one to two days earlier than previously. Vomiting babies are regarded as presenting too difficult a problem to treat locally for longer than three days, and are now sent to Perth after that period. One baby's life was certainly saved; the case of supraventricular tachycardia superimposed on a neonatal infection was not diagnosed locally, because I did not reexamine the baby. The diagnosis was made and treatment was successfully carried out at Princess Margaret Hospital.

Consultants.

Consultants continue to be the centre around which all the more academic advances in general practice must revolve.

Telephone consultation in neonatal problems poses extreme difficulties to the consultant pædiatrician, owing to the critical nature of the evidence to be obtained, and to the difficulty experienced by the general practitioner in finding that evidence for him. It can be very painful to find out how little one has searched for the vital evidence needed to establish a diagnosis. This is the chief value in constant team-work—the knowledge that the consultant has to ask awkward questions. However, there is a considerable temptation to fabricate answers, particularly if the physical examination has been incomplete. If the evidence has not been elicited one must hang up the telephone and return to the bedside for a further examination.

The exact diagnosis was made in seven out of thirteen consultations in the seriously ill neonatal and post-natal groups. Three of the cases should have been diagnosed

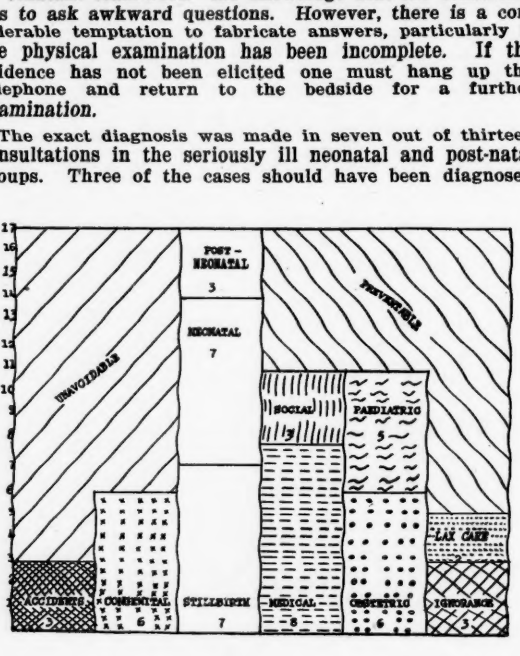

FIGURE I.
Cause of fœtal deaths.

(diaphragmatic hernia, intraperitoneal hæmorrhage, and B. coli meningitis). In another three post-mortem examinations were needed to establish the diagnosis (unilocular heart, staphylococcal septicæmia, and patent interauricular septum).

The types of case in which an obstetrician was telephoned were as follows: all proposed Cæsarean sections and many difficult labours; five cases of toxæmia; two cases of fourth-stage hæmorrhage; one case of death *in utero*.

The ages of those consulted ranged from thirty to sixty years. In the difficult obstetrical problems nine different consultants have been telephoned about 18 varying emergencies; without exception the advice given was conservative, in full detail, and adequate. It was they who determined the 1·2% Cæsarean section rate. It is of interest that this corresponds with the present 1·8% Cæsarean section rate among public patients at the King Edward Memorial Hospital (Mathew, 1955). However, the general practitioner must not become annoyed if he has evidence that the consultants are not so conservative in their private practices (private Cæsarean section rate, King Edward Memorial Hospital, 3·6%). In view of the ease of performance of Cæsarean section, public opinion always expects the specialist to be successful. The constant "special" case in which the patient is just coming into labour, and other factors, make this figure of 3·6% very reasonable by world standards (particularly in relation to the United States of America).

It is also to the consultants' credit that they were willing to give information on their bad results—a very valuable source of information to the general practitioner who carries out certain procedures only occasionally. None

TABLE III.

Details of 17 Stillbirths and Neonatal and Post-Neonatal Deaths.

Type of Death.	Avoidable or Not.	Cause of Death.	Comments.
Stillbirth.	Avoidable.	Obstructed labour.	Persistent posterior presentation; post-maturity; poor judgement.
Post-neonatal.	Avoidable.	Pneumonia at three months.	Severity under-estimated.
Stillbirth.	Avoidable.	At 30 weeks; mother unmarried.	"Landed on doorstep"; social factors.
Stillbirth.	Avoidable.	Pre-eclampsia.	Lax care; adequate warning.
Neonatal.	Unavoidable.	Accident to mother.	Fœtal leg amputated at 29 weeks.
Stillbirth.	Avoidable.	Chronic nephritis.	Social factors; no care; accidental hæmorrhage.
Neonatal.	Avoidable.	Premature, 32 weeks.	Heavy dairy work; social problem.
Neonatal.	Avoidable.	Bacterium coli meningitis.	Precipitate labour; tentorial tear; slow diagnosis.
Neonatal.	Unavoidable.	Diaphragmatic hernia.	Kicked in abdomen by cow at 20 weeks; infant delivered at full term.
Neonatal.	Avoidable.	Hæmorrhagic diathesis.	Slow treatment; intraperitoneal hæmorrhage.
Post-neonatal.	Avoidable.	Gastro-enteritis, five weeks.	Condition under-estimated.
Stillbirth.	Avoidable.	First-stage distress.	Failure of conservative care; poor judgement.
Stillbirth.	Unavoidable.	Accident to mother.	Mother bunted in abdomen by heifer; fœtus macerated.
Neonatal.	Unavoidable.	Congenital heart disease.	Patent auricular septum; 24 hours old.
Neonatal.	Unavoidable.	Congenital heart disease.	Unilocular heart; 48 hours old.
Post-neonatal.	Unavoidable.	Staphylococcal septicæmia.	Found dead in bed by mother; six months old.
Stillbirth.	Avoidable.	Accidental hæmorrhage.	Lax instructions in ante-natal care.

appeared to give way to their alleged bias towards a particular form of unorthodox treatment.

The Management of Labour.

The management of labour has continued to be conservative, with stress on the ante-natal care, education and preparation of the patient. In this series of cases the *Cæsarean section rate was 1·2% and the fœtal wastage* was 2·2%; 28% of 540 labours were in *primigravidæ*.

In one in five cases a version was performed, episiotomy was performed in 23%, manual removal in 1·5%, and forceps delivery in 4·1%. The morbidity rate was 9%, and *toxæmia occurred in 3·2% and breech presentation in 1·8%.*

It is of interest to sample current trends in other hospitals. *Townsend (1954) at the Women's Hospital*, Melbourne, observed a Cæsarean section rate of 2·69% with a stillbirth-neonatal wastage of 3·6% in the period 1952-1953. *Jeffcoate (1953) in Liverpool during 1951, receiving* a high proportion of abnormal cases, had a 13% Cæsarean section rate and 17% forceps delivery rate with a fœtal wastage of 3%. Jameson and Handfield-Jones (1954) in a cottage hospital in Gloucestershire had a 1·1% Cæsarean *section rate and 15% forceps delivery rate with 3% fœtal* wastage. Hopkins (1955) in Queensland gives a Cæsarean section rate of 3·8%, a forceps rate of 32%, and 2·2% fœtal wastage. At the *King Edward Memorial Hospital (1954-1955)* an analysis of the public cases showed a Cæsarean *section rate of 1·8%, a forceps delivery rate of 3·8%*, and a fœtal wastage of 3·5%. The corresponding figures in the private cases were as follows: a Cæsarean section rate of *3·6%, a forceps delivery rate of 10·4%, and 3·9% fœtal* wastage. Salzmann (1955) noted a Cæsarean section rate of *0·6%*, a forceps delivery rate of 4·1%, and a fœtal wastage of 3·6%.

The position of forceps deliveries invokes no basic controversy (Townsend did not bother to publish his forceps delivery rate). Provided that a first-class anæsthetic and competent application of the forceps are obtainable, rates varying between 4% and 33% do not indicate any radical difference in the management of labour. The use of episiotomy falls into much the same category. A low forceps delivery rate of 4% has been deliberately chosen in this series in view of the anæsthesia available, adequate ante-natal training of the mothers, and my own modest experience. Recently another medical practitioner has been called in to administer cyclopropane in forceps deliveries. This reverts to DeLee's maxim that two doctors should be present for maximum safety in any confinement.

No records have been kept of the duration of labours, of minor accidents during the ante-natal period, or of the incidence of uterine inertia. The classification of inertia has undergone considerable changes since the onset of this series, and the trend of opinion has been to shorten the time of "normal" labour by definition. Definite limits are being suggested—*thirty-six hours for the duration of* labour (Kennedy, 1955) and two hours for the second *stage, regardless of the absence of maternal or fœtal* distress. In this practice these limits could be used only as a rough guide, as the time of onset of labour or of the *second stage is rarely known with sufficient accuracy.*

The Cæsarean section rate is undoubtedly the main *indication of conservatism* or otherwise. It would appear that the current Australian rate is about *3% in a well-*equipped hospital service. It can be categorically stated *that the conditions of adequate maternal or fœtal safety* are not fulfilled in this hospital in any one aspect of the performance of Cæsarean section—for example, anæsthesia, *surgical experience, transfusion services, neonatal resuscitation*, care for thrombotic complications associated with the operation, or expert pædiatric supervision of the infant in the neonatal period. In this practice *maternal safety* takes prior consideration, and a conservative outlook has *resulted in a low Cæsarean section rate (1·2%)* with a probably increased risk to the fœtus (not yet reflected in the mortality figures). It is difficult, on account of the *distances in Australia, to see how these basic weaknesses* in the management of Cæsarean section will be changed. This, of course, does not mean to say that we do not take all possible precautions. *It merely indicates that any large* increase in Cæsarean section rates will inevitably increase *maternal mortality under present conditions* in hospitals of the size with which I am dealing.

Radiology and Ante-Partum Hæmorrhages.

The conservative management of ante-partum hæmorrhage *is undoubtedly of great benefit to the country practitioners*, and must rank in importance with the intravenous use of ergot in the third stage of labour.

During the years 1953 and 1954 it has been possible to examine radiologically all patients with moderate to severe *ante-partum hæmorrhage, to attempt determination of the* placental site. Three patients have been sent to Perth, and latterly two patients have been satisfactorily examined locally, the films being sent to a radiologist. The quality of the films was poor on two other occasions. The X-ray *examination is repeated, and if the films are still poor* the patients are sent to Perth. It is important that the decision be left to a consultant except in an extremely rare emergency, and a report can *usually be obtained in* forty-eight hours. It cannot be stressed too much that these technical advances in the country hospitals should be used to gain further information which will draw the practitioner into closer contact with the consultant—not *make him more independent of outside opinions.* Radiology is an excellent example of this principle. One patient, an Italian migrant, underwent an elective Cæsarean section on *purely radiological grounds.*

An important gap in the treatment of catastrophic hæmorrhages has been filled by the storage of dextran and fibrogen near the labour ward.

Procedures Found to be Impracticable to Date.

Heroic manipulative procedures in vaginal delivery have not been used at all. The bewildering set of instruments, many of historical interest, studied when I was a student, appears to be unfashionable and not needed. One cannot doubt that these instruments will occasionally be needed, but the rule followed in this practice has been as follows: any procedure that may produce severe maternal lacerations through the use of an unfamiliar instrument should be abandoned in favour of Cæsarean section.

To date I have not plucked up courage to use the continuous intravenous drip administration of "Pitocin" drip throughout labour; the reason is inadequate theoretical knowledge of uterine inertia. No members of the staff have been trained in its use, and I await further large case reports before adopting it.

Hypnosis has not been undertaken in any further cases, in view of the time taken to train the patients. (Two cases were recorded in the first report.)

With regard to fœtal electrocardiography, a pre-amplifying circuit was constructed for me by Philips Electrical Industries, and successful tracings were achieved from four out of four thirty-eight week pregnancies. The method is time-consuming, and further enthusiasm will probably follow technical advances which eliminate maternal skin interference.

Staphylococcal Infections and Laboratory Control.

It has been shown in England that there is a much greater incidence of staphylococcal infections among infants delivered in hospital than in domiciliary practice. This hospital has been no exception, and in 1953 the small bacteriological laboratory was formed as a further measure to limit cross-infection.

Routine examination of nasal swabs from members of the medical and hospital staff has been performed for the first time. Six persons out of a staff of 26 were detected as nasal carriers of *Staphylococcus aureus*. Examination of swabs taken in the laundry revealed a potent source of infection, and a minor revolution in laundry methods has resulted.

One now knows more, and each outbreak has been controlled more rapidly. Breast abscesses occurred in 9% of the last 200 pregnancies, mainly after the patients had left hospital. The total hospital morbidity (9·2%) is in the same category as Calman and Gibson's (1953) finding of 7% at Queen Charlotte's Hospital in 1951. It would appear that the incidence of breast abscesses has increased over previous years at a time when less than 10% of staphylococci are penicillin-sensitive. No staphylococci insensitive to "Terramycin" have been detected to date.

Establishing a Small Country Hospital Laboratory.

This small laboratory has proved an outstanding success. Previously, one small room with no running water had been available; it contained a microscope and the usual collection of ill-fitting test tubes for the centrifuge, uncleaned slides, dried Gram stains and empty bottles. The few hospitals that I have seen seem to possess such a room, containing the microscope from student days.

After considerable experimenting, the objects of the laboratory were limited to those that could be carried out expertly by a partly trained technician.

The following items were purchased by the Hospital Women's Auxiliary or supplied by the Government Health Department: one incubator, costing £68; one electric centrifuge, cost unknown; adequate supplies of sterile test tubes, ready packed in wooden containers for mail transport; spirit stoves, tripods and other minor laboratory aids—for example, disposable tissues, adequate test-tube racks.

With regard to cultures, the staphylococcus is considered to cause the great majority of the therapeutic problems. Blood agar medium was discarded in favour of serum agar, which can be stored for months, a few plates poured at a time keeping well in a refrigerator. The staphylococcus thrives on serum agar, as do many other common organisms. The sensitivity disks used were penicillin, streptomycin and "Terramycin". As well as the tests performed as a routine measure on plain agar were coagulase tests confirming the presence of pathogenic organisms; but no attempt is made further to confirm the nature of the organism, other than by observation of colonies and clinical evaluation. Two main facts are required—first, the probable nature of the organism, and secondly, its antibiotic sensitivities.

The technicians received a month's basic laboratory instruction at the Royal Perth Hospital laboratories, in the collection and plating of specimens, destruction and preparation of plates, incubator maintenance and laboratory cleanliness. These technicians have been technically and educationally unqualified except for this basic training. However, there has been a constant problem of high technician turnover, and the present modest two months' training in X-ray and laboratory work appears the only practical solution devised to date. However, this is a considerable advance for a 50-bed district hospital. The bulk of the remaining duties of the technician are to collect and pack specimens adequately for transport to the Public Health Laboratories, and to maintain a clean laboratory.

Although this laboratory is a very modest affair, the discovery of our first successful culture and sensitivity test carried out locally was a very exciting moment in its development.

The Influence of Social Conditions upon Mortality.

Social and regional factors in mortality exert independent actions, and there is a considerable time lag in their expression (Daly *et alii*, 1955). McNamara (1952) in Missouri found that sampling as few as 200 families in a relatively homogeneous population was adequate for reliable estimates in morbidity, significantly higher morbidity rates being found in the lower socio-economic rankings.

The difference in country and metropolitan mortality rates observed to 1951 has continued to 1954, particularly in neonatal and post-neonatal deaths. Country and metropolitan stillbirth rates are now approximately the same in most States. Country people tend to have larger families, and this fact is related to a higher postnatal death rate. The three postnatal deaths occurred in 177 families of three children and over, whilst no postnatal death occurred in 171 families of two children and under. Of the farm families 55% had three or more children, compared with only 45% of town families. This confirms Daly, Heady and Morris's (1955) findings. However, no attempt has been made to group these families into the five social occupational classes used by the British General Register Office.

In this dairying district, the two major groups were the farming and non-farming occupations, in which considerable average differences in income, type and hours of work, and living standards were recorded in 1953 by Schapper. He found that 20% of farmers had net incomes of £300 per year or under, whilst 50% earned less than £530 *per annum*. Living conditions were generally poor, and there were few household facilities and amenities. Of farm homes, 17% had not running water, electric light, washing machines, refrigerators or telephones, and only 7% had all these. About one-third of the wives helped in the milking shed.

It is interesting that some of these wives regarded their confinement in the maternity hospital as their holiday.

No accurate records of country town living standards are available. However, for the majority net incomes after the rent has been paid must be at least £500. Over one-third of the houses have been constructed since 1947, and all have electric light and running water, with compulsory septic tank sewerage.

In this survey there were eight combined deaths amongst the 192 town families, compared with nine deaths amongst the 156 farm families. The evidence here suggests that the differences observed between the metropolitan and country neonatal and postnatal death rates are partly due to the

effect of the poorer farm sociological conditions and larger farm families. It would be of great interest for State Government statisticians to divide a large series of cases into three groups instead of the present two—namely, metropolitan, country town and rural—as the reasons for persisting social differences in mortality are at present imperfectly understood. However, there is considerable evidence that even in the farm groups there has been a remarkable improvement in social conditions, and that the dominant factors in mortality are medical and not social.

In this district there appears to be no limit to the advice most patients can take in their own interest. This is probably a new sociological effect of raised living standards and is in contrast to former decades. This is another indication of the academic nature that general practice is assuming. One glance at the incidence of complications reveals the frequency of major or minor abnormalities; over 45% of all patients presenting were given some therapy during their antenatal or postnatal care. Neonatal pædiatrics is highly academic, and skilled diagnostic intervention has been required in one in every 30 cases. Better social conditions, and hence lower mortality rates, have made rarities comparatively commonplace, and the traditional causes of mortality (for example, malnutrition) are not so common. In view of present trends, it is disturbing to know that if a medical career of 2000 confinements includes either one maternal death, one case of eclampsia or one case of ruptured uterus, the unavoidable rate of incidence will have been exceeded.

Further improvements in social conditions will tend only to accentuate the relative importance of the hard core of academic problems.

Summary.

The preliminary fall in fœtal mortality reported in 1953 has been confirmed in an additional 215 cases. In the total of 515 cases, the expected Western Australia country loss was 23·7 and the observed loss was 14 among booked patients. The loss among 25 unbooked patients was three. This deviation from expectation is significant at the 5% level.

The causes of the preventible deaths were analysed into four groups, as follows: difficult confinements, three; lax care, two; inadequate assessment of the critical nature of the illness, three; sociological causes, three. Accidents to the mother played a contributory role in five deaths. A notable omission from the stated causes of death was poor nursing.

Rural weaknesses in pædiatric care have been analysed, and measures to improve this service have been carried out. In seven out of 18 cases of cyanosis reported from the nursery the babies died from varying causes.

The importance of consultants' aid is stressed.

The observed complications in this series are compared with current trends in other hospitals. Evidence is presented on the desirability of maintaining the present low Cæsarean section rate.

The preliminary experiences in radiological investigation of antepartum hæmorrhages are detailed.

Certain procedures have been discarded (heroic manipulations, hypnosis) or have been found to be as yet unsuitable (intravenous drip administration of "Pitocin", and fœtal electrocardiography).

Stress is laid on the success of a small bacteriological laboratory established in 1953, and details are given of the problems involved in its formation and management. One partly trained technician has been doing the combined job of X-ray and laboratory work.

Evidence is presented in studies of 348 families to show that the continued differences in rural and metropolitan mortality rates are due in part to the poorer farm social conditions and larger farm families.

Probably for the first time in history, socio-economic factors are a minor cause of mortality, and the majority of preventible fœtal deaths may be dependent upon the academic skill of the practitioner.

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MALIGNANT TUMOURS IN MELANESIANS.

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DURING a period of eighteen years, from 1923 to 1940, the writer examined material from 83 malignant tumours in full-blooded Melanesian natives. Twenty-one of the specimens were derived from autopsies, of which 1541 were performed at Rabaul during that period. Of the remaining 62 specimens, 24 were from biopsies from the Native Hospital, Rabaul, 21 were autopsy and biopsy specimens from native hospitals elsewhere in the Territory and 17 were submitted by medical officers of missions.

Of the 21 specimens from autopsy in Rabaul, 15 were classed as carcinoma and six as sarcoma. The biopsy specimens provided a similar proportion of carcinomata, the preponderance of epithelial tumours being due chiefly to those occurring on the leg following chronic ulcer, in the mouth, and as primary neoplasms of the liver.

Included in the figures shown in Table I are one case already reported by Deland *et alii* (1933), one by Price (1940) and five of the series of 10 reported by Penington (1933) encountered during a period of about eighteen months. Dr. Penington's successor, Dr. C. S. James, saw, during a period of three years, seven tumours from the same locality, amongst villagers of the Rabaul district of New Britain.

These details of the source of material are given for what slight bearing they may have on the prevalence of malignant disease in these natives.

In regard to autopsies at Rabaul, the proportion of adult male to female subjects was of the order of 10 to one, and the majority of the former would be aged between twenty and thirty years. Specimens from males would also predominate in biopsy material from native hospitals. Mission doctors would see more representative samples of the

native village communities; Penington's 10 patients included four adult females, and the seven examined by James were four adult males, two adult females, and a child, aged two years. Many natives of all ages and both sexes were, of course, examined during medical patrols, and some of the patients subsequently reaching native hospitals may have been sent in as a result. Under such conditions only obvious external tumours would be seen, and some of these would be concealed if possible.

The 83 tumours are classified according to histological type and site in Table I.

Comment on Some Epithelial Tumours.

It will be noted that 19 of the 28 squamous-celled cancers involved the buccal cavity or the extremities. In regard to the first-named site, the question of betel-nut chewing naturally comes up. Penington (1933) discusses this factor in relation to three of his patients, two of whom were females. Indian writers have stated (Khanolkar, 1950) that betel-nut chewing does not cause cancer unless tobacco is chewed as well.

The matter is discussed at some length by Kouwenaar *et alii* (1951). These authors quote figures indicating an unduly high proportion of mouth cancers in women. It is also stated that although in Java the habit of betel chewing is widespread in both sexes, in Sunda it is practised more by women than by men. In 1937, of 11 Javanese patients with mouth cancer, eight were men and three women, whereas of nine Sundanese patients, six were women. However, in most of the available figures data bearing on this suggestive difference were lacking, and the problem remained unsettled.

Penington (1933) gives the composition of the betel-nut "quid" as areca catechu, slaked lime and the fruit of a "pepper-vine", the last-mentioned of which may not be the same species in all districts; he states that tobacco was not commonly chewed. The writer has nothing to add to these remarks.

The leg cancers had supervened on chronic tropical ulcer, which was, and probably still is, one of the commonest causes of admission to hospital in the Territory. Here caution is needed, since, as ten Seldam (1953) has pointed out, an ulcer which, on the histological picture, would be pronounced squamous carcinoma, may remain quiescent for many years and produce no metastases. In five cases of the present series, including cancers of the arm and sole of the foot, in which there was an antecedent history of a yaws-like lesion, it must be admitted that the diagnosis rested on the histological findings. Of the remaining five cases, in three there was extensive invasion of underlying bone (with spontaneous fracture of the tibia in one case), but there is no record of metastases, while in both of the remaining two there were metastatic deposits in inguinal lymph glands and in one extensive bone invasion had occurred. Leaning somewhat on Willis's description of local spread and the metastasizing potentialities of skin cancer (1948), the writer prefers to retain all 10 cases in their present category.

Conjunctiva.

Cancer of the conjunctiva is rare in man, but said to be common in some domestic animals, particularly the horse (Willis, 1948). Stout (1932) quotes Judd (1929) as having stated that in reporting a case he could find records of only 20 others. However, Dr. R. E. J. ten Seldam has drawn the writer's attention to a paper by Muller (1939), in which neoplasms of the corneal limbus in 13 Javanese adults are described. Of these, eight are listed as carcinoma and four as malignant papilloma. These patients came under observation during a period of nearly four years, and Muller states that the condition is no more frequent amongst the Javanese than it is in Europeans.

In view of the comparative rarity of the condition, brief notes of the two Melanesian cases are given.

CASE I: K207/29. The patient was an adult male native of Kavieng, New Ireland. The specimen, consisting of an enucleated eye, was sent by Dr. E. J. Ryan, who described a mushroom-shaped growth about three-quarters of an inch in diameter with the base apparently attached to the cornea and the inner part of the sclera of the right eye. The growth was said to have been of two years' duration.

TABLE I.

Classification of 83 Malignant Tumours from Melanesian Natives.

Histological Type and Site.	Number of Cases.	Remarks.
Epithelial tumours:		
Squamous-celled carcinoma:		
Buccal cavity (excluding lip and tongue)	9	7 adult males, 2 adult females.
Lip	2	Adult males.
Tongue	2	Adult males.
Conjunctiva	2	1 adult male, 1 adult female.
Leg	8	5 adult males, 3 females.
Sole of foot	1	Adult male.
Arm	1	Adult female.
Breast (epidermoid cancer invading deeply)	1	Female.
Cervix uteri	1	
Penis	1	
Total	28	
Basal-celled carcinoma (face)	1	
Glandular carcinoma:		
Liver (primary)	6	Males.
Liver (secondary nodule, primary growth not seen)	1	Adult male.
Gall-bladder	1	Adult male.
Stomach	2	Adult males.
Colon	1	Adult female.
Bronchus	1	Adult male.
Thyroid	1	Adult male.
Parotid	1	Adult male.
Uterus (body)	1	
Breast (*carcinoma simplex*)	1	
Vertebræ and lung (secondary to hidden focus, possibly in prostate)	1	Adult male.
Total	17	
Other cancerous tumours:		
Melanoma (foot)	1	Adult male.
Glioma group (retina)	2	1 male child, 1 female child.
Seminoma testis	1	Adult male.
Carcinoma of ovary	1	Adult female.
Anaplastic tumour of palate (filling mouth)	1	Adult male.
Anaplastic tumour of orbit (extensive)	1	Adult male.
Carcinoma of axilla (large encephaloid mass)	1	Adult male.
Carcinoma of pelvis (scirrhous mass, extensive)	1	Adult male.
Chorioncarcinoma	1	
Total	10	
Tumours of connective and lymphoid tissue:		
Lymphosarcoma	7	6 males.
Round-celled sarcoma	5	4 males.
Spindle-celled sarcoma	5	Males.
Giant-celled sarcoma	2	Males.
Hæmangiosarcoma	1	Female infant.
Type not defined	5	
Total	25	
Other malignant tumours:		
Malignant teratoma	1	Male child.
Mixed parotid tumour	1	Adult male.
Total	2	

Vertical antero-posterior section through the tumour and the eyeball showed the cornea to be completely covered by a mass of greyish-white tissue up to five-eighths of an inch thick, and extending from a point about half an inch medial to the inner corneo-sclerotic junction to the outer corneo-sclerotic junction. The posterior surface of the cornea appeared to be intact and all structures within the eyeball in normal relationship. Microscopic examination of the mass showed it to consist of squamous epithelium irregularly partitioned by a scanty stroma and showing some imperfectly cornified "cell nests" In the base of the growth there was dense round-celled infiltration, extending in parts between the superficial strata of the cornea, and some dilated blood vessels and hæmorrhages were present. Otherwise there was no sign of deep extension of tumour cells.

CASE II.—C/1471/35. The patient was a female native of New Britain. An enucleated eye was sent by Dr. C. S. James, whose note stated that about fourteen months previously a small seed-like swelling had appeared on the cornea. This was said to have been removed on two occasions, but to have returned and continued to grow. On examination, the whole cornea was covered by a pinkish, slightly pedunculated excrescence projecting about a quarter of an inch from the surface of the eye. On section of the eye the mass was entirely extraocular. Microscopic examination showed it to consist of squamous epithelium. It was more vascular than the tumour in the previously cited case, and there was more complete cornification of "cell nests". No penetration of the cornea had occurred.

Cancer of the Liver.

Primary cancer of the liver is now a well-known phenomenon in African and Asiatic peoples. Its possible ætiology is discussed by Kouwenaar (1950). More or less advanced cirrhosis commonly precedes the neoplasm. In one of the present series of six cases the tumour was of recent origin, presenting a small globular swelling projecting from the surface, just to the left of the round ligament, of a small contracted "hobnail" liver. One case occurred in a boy whose age was not more than fourteen years. Advanced cirrhosis of the liver, apart from malignant disease, was encountered six times in 1050 native autopsies. The animal parasites commonly associated with liver cirrhosis (schistosomes, *Clonorchis sinensis*) in some countries have not been found in Melanesian natives, who have no fermented beverage of their own, and only a few have occasional access to imported liquor.

Conclusion.

Although many of the remaining tumours are individually interesting, it is not proposed to make further comment, since the purpose of this paper was simply to record the number and main types of neoplasm seen over a given period and ending at the year 1940. As it is, the writer has exceeded his intention by citing later literature, and this threatened to lead further afield and also to further procrastination. The story of malignant disease in Melanesia must now be taken up by others.

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THE RAPID MEASUREMENT OF VENOUS PRESSURE IN THE LEGS.

By BARTON VENNER, M.S., F.R.C.S., F.R.A.C.S.,
Adelaide.

THE normal pressure of the blood in the veins of the legs at rest is approximately equal to that of the column of blood supported in those veins, below the level of the right atrium. This is true of both normal and varicose veins. However, during walking there is normally a fall in the pressure, as the valvular system of the veins is invoked to promote the flow of blood towards the heart. If these valves are incompetent, no such fall in the pressure occurs; and if there is actual venous obstruction, the pressure may rise.

Various tourniquet tests on patients with varicose veins have been described to illustrate these pressure variations by the visible filling of the veins. The actual measurement of the pressure can be used as an adjunct to these tests, and to supplement venography in those cases in which a fuller investigation is required.

The method to be described for measuring the venous pressure in the legs is a modification of the technique used by Walker and Longland (1950) in their investigation of these pressure changes. It does not claim to be as accurate as was theirs, although the use of a water column instead of mercury as a manometer has the advantage of magnifying the scale of pressure changes. This allows the rapid detection, in the surgery, of those patients who have diseased and incompetent deep channels.

The pressure is measured quite simply by balancing it against a free column of liquid in a flexible tube, one end of which is inserted into the desired vein.

Apparatus.

The requirements for the method are two hypodermic needles (size G18 are best), a seven-foot length of soft "Latex" tubing, syringe barrel of 20 cubic centimetres' capacity, and 50 cubic centimetres of citrated normal saline solution.

The butt end of one needle is inserted into one end of the length of tubing and bound with thread. The other needle is passed point first into the other end of the tubing and its butt end is similarly bound, so that it can be used to attach the syringe barrel.

Method.

With suitable aseptic precautions, the syringe barrel is attached to the tubing and the whole is filled with saline solution, while both ends are held at the same level.

The patient is made to stand, and the largest accessible vein on the dorsum of the foot is selected. Then, while an assistant holds the syringe barrel at the patient's head level and pinches off the tubing, the needle at its other

end is inserted into the vein, and at once secured by a piece of elastic adhesive strapping.

The tubing is then released, when the solution will begin to flow, and its level will fall to a height from the floor corresponding to the pressure in the patient's vein. The fluid level is readily visible in the tubing, and can be measured with reasonable accuracy by this height, or roughly in relation to the patient's body. If desired, the syringe can be lowered in such a way that the fluid level remains in the glass barrel rather than in the tubing.

By the use of the slack in the tubing, the patient can now be asked to walk, or even run "on the spot", while the fluid level is observed. Normally, a prompt fall to a new level will occur; the level may remain unchanged, or rarely a rise will occur.

The tests may be repeated after the application of tourniquets to the leg, and if desired the procedure can be completed by the use of the lowermost half-inch of the tubing to inject a radio-opaque substance for the making of venograms.

Reference.

WALKER, A. J., and LONGLAND, C. J. (1950), "Venous Pressure Measurements in the Foot in Exercise as an Aid to Investigation of Venous Disease in the Legs", *Clin. Sc.*, 9 : 101.

THE MORTALITY IN AUSTRALIA FROM LEUCHÆMIA.

By H. O. LANCASTER,
School of Public Health and Tropical Medicine, Sydney.

THIS paper summarizes the information in *Demography*, the annual bulletin of the Bureau of Census and Statistics, Canberra, on the mortality from leuchæmia and Hodgkin's disease in Australia.

Definitions.—The term "leukæmia" includes all forms of leuchæmia, without subdivision into clinical types. The term "aleukæmia" was used over the years of this survey as synonymous with Hodgkin's disease, a usage that has been abandoned in the sixth decennial revision of the "International List of Causes of Death". "Aleukæmic leukæmia", however, would be referred to the rubric "leukæmia". Before 1920, the two diseases leuchæmia and Hodgkin's disease were not differentiated in the official statistics. These points are discussed in detail in "Epidemiological and Vital Statistics Report" (1955).

Leuchæmia.

The death rates in Australia from leuchæmia are given in Table I by age and sex. In any period, the death rates are relatively high in the first few years of life and then decline to a minimum over the years of young adult life, fifteen to forty-four years. From about forty-five years onwards the rates increase up to seventy-five years, above which there is a decline. This decline in the age group over seventy-five years may be an artefact due to the increasing efficiency of diagnosis, which would first have been apparent in the younger age groups and would now affect increasingly older age groups. In any case, it seems to be less evident if the rates are examined on a generation method. For example, the males have a mortality of 49 per million *per annum* at ages sixty-five to seventy-four years, in the period from 1921 to 1940, and then ten years later the mortality rate of the same group of persons would be 53 per million, and this group of persons would be in the age group seventy-five years and over. Similarly, the males aged sixty-five to seventy-four in the period from 1931 to 1940 have a death rate of 97 per million *per annum*, and ten years later the same group has a mortality of about

$$\frac{81 + 127}{2}$$ or 104 per million *per annum*.

It does not seem possible to disentangle the "generation" effects from the changes in diagnostic efficiency.

In Table II the importance of leuchæmia as a cause of death is noted. Only in the school years, five to fourteen years, does the disease attain an important numerical proportion of the deaths. There is a high masculinity at all ages except thirty-five to fifty-four years.

TABLE II.
Leuchæmia in Australia from 1931 to 1940.

Age (Years).	Deaths from Leuchæmia as a Percentage of all Deaths.		The Masculinity of the Death Rates.
	Males.	Females.	
0 to 4	0·30	0·32	119
5 to 14	1·65	1·48	153
15 to 24	0·75	0·73	133
25 to 34	0·60	0·34	178
35 to 44	0·36	0·43	100
45 to 54	0·34	0·44	106
55 to 64	0·26	0·29	136
65 to 74	0·19	0·17	152
75 and over ..	0·04	0·04	120
All ages	0·28	0·27	132

The most comprehensive clinical survey of leuchæmia is that of Gauld, Innes and Robson (1953); but in comparing their data with the Australian data it should be noted that they are dealing with deaths not related to a population at risk. It is evident from their work that the higher rates in infancy are due to acute lymphatic leuchæmia, and that the bulk of later deaths are due to chronic lymphatic and chronic myeloid leuchæmia. It would appear also from their graph that the death rates from acute myeloid and monocytic leuchæmia increase throughout life.

TABLE I.
The Mortality in Australia from Leuchæmia.

Period.	Sex.	Deaths per Million *per Annum* at Ages (Years).									
		0 to 4.	5 to 14.	15 to 24.	25 to 34.	35 to 44.	45 to 54.	55 to 64.	65 to 74.	75 and Over.	All Ages.
1908 to 1910[1]	M.	25	14	14	9	9	34	39	41	33	18
1911 to 1920[1]	M.	21	18	17	17	16	32	45	57	25	22
1921 to 1930	M.	23	17	10	10	14	22	38	49	25	18
1931 to 1940	M.	38	23	16	16	16	33	57	97	53	29
1941 to 1945	M.	49	20	(15)	(12)	24	46	67	112	81	34
1946 to 1950	M.	51	31	24	23	23	54	94	159	127	47
1908 to 1910[1]	F.	18	6	8	4	16	18	29	11	13	11
1911 to 1920[1]	F.	16	8	8	12	19	19	32	39	12	14
1921 to 1930	F.	21	10	9	9	17	25	55	40	25	16
1931 to 1940	F.	32	15	12	9	16	31	42	64	44	22
1940 to 1945	F.	39	16	15	16	17	31	71	81	61	29
1946 to 1950	F.	43	24	14	17	24	41	82	115	88	38

[1] Includes Hodgkin's disease.

TABLE III.

The Mortality in Australia from Hodgkin's Disease and Related Diseases.

Period.	Sex.	Deaths per Million *per Annum* at Ages (Years).									
		0 to 4.	5 to 14.	15 to 24.	25 to 34.	35 to 44.	45 to 54.	55 to 64.	65 to 74.	75 and Over.	All Ages.
1908 to 1920						Included in leuchæmia					
1921 to 1930	M.	5	7	10	10	12	17	26	35	22	12
1931 to 1940	M.	3	4	6	11	17	20	33	31	38	13
1941 to 1945	M.	4	5	7	9	16	19	26	36	25	12
1946 to 1950	M.	1	4	7	13	16	21	31	48	40	15
1921 to 1930	F.	2	3	5	6	6	10	28	20	7	6
1931 to 1940	F.	2	1	6	6	7	10	20	18	26	7
1941 to 1945	F.	1	0	4	9	11	16	19	33	17	10
1946 to 1950	F.	1	1	2	7	9	18	17	30	26	9

Hodgkin's Disease.

In Table III are given the death rates from Hodgkin's disease. For any period there is a tendency for the rates to increase with age, and there is a high masculinity. The rates have remained at roughly the same levels over the whole of the years of the survey.

Acknowledgement.

This paper is published with the permission of the Director-General of Health, Canberra.

Reference.

"Epidemiological and Vital Statistics Report" (1955), 8: 81, World Health Organization.

GAULD, W. R., INNES, J., and ROBSON, H. N. (1953), "A Survey of 647 Cases of Leukæmia, 1938-51", *Brit. M. J.*, 1: 585.

Reviews.

Clinical Bacteriology. By E. Joan Stokes, M.B., B.S., M.R.C.P., M.R.C.S., with a foreword by A. A. Miles, C.B.E., M.D., F.R.C.P.; 1955. London: Edward Arnold (Publishers), Limited. 9" × 5½", pp. 296, with 25 illustrations. Price: 20s.

HERE is still another in the long procession of clinical diagnostic laboratory manuals. Miss Stokes has produced an eminently readable small volume containing a large amount of sound sense, practical detail and a critical approach to the consultative aspect of diagnostic work. So often the clinician with a conviction as to what the laboratory should find tends to think there has been a technical failure when the desired result does not appear. This work is ready with many explanations for such a situation, and the means to explore it, and to prove or disprove the techniques used. The opening chapters, in the words of Dr. A. A. Miles, have something of the academic approach which often is the hall-mark of good practice. That is, they display a critical approach to the evidence obtained in laboratory findings, and are a warning against false reasoning which often proceeds from the wish to begin treatment immediately.

The essential differences in material from sites normally sterile, contrasted with those from regions with a normal flora, are emphasized in the description of gathering and transport of such material. The sight of dried, insufficiently large samples and the impossibility of repeating them is all too well known to the routine diagnostician, and so the details given here are of real value. The "transport medium" for gonococcus swabs is not well known in this country, but should prove excellent for samples collected at a distance from the laboratory.

The routine identification of bacteria is set out in sufficient detail for clinical diagnosis. The description of Fuller's method for grouping hæmolytic streptococci is accompanied by a useful diagram. In Australia, we are more accustomed to use the Ward and Rudd maltose plate as being quicker and calling for less laboratory manipulation to recognize human pathogens. One point of contention arises in the use of a toxin production *in vitro* method as a test of the virulence of *Corynebacterium diphtheriæ*. Some of this work was done in Australia, and we are familiar with the many small difficulties which can disturb this technique, and would suggest that the day has not yet come when the guinea-pig can be dispensed with.

The technique for testing combinations of antibiotics against a patient's own organism, too, may be fraught with difficulties. Such results can be offered only as tentative information to the clinician, because there are so many other variable factors in the living patient.

The chapter on cross-infection illustrates the modern recognition of the perils of hospitalization and describes the ways in which they can be minimized. However, the suggestion of the insufflation of penicillin sulphonamide powder into the nose carries another peril for the patient—that of sensitization to these drugs, and one to be carefully avoided—this will most surely disappear from the next edition.

The book is well set out and pleasantly printed by Edward Arnold and Son.

Medicine for Nurses. By M. Toohey, M.D., M.R.C.P., D.C.H., with a chapter on Psychological Medicine by Henry R. Rollin, M.D., D.P.M.; Second Edition; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 8¼" × 5¼", pp. 656, with 180 illustrations. Price: 28s.

THIS book, now appearing in its second edition, is far more comprehensive than many similar books written for nurses, and will fulfil the hope expressed in the preface, that it may prove a useful work of reference for trained nurses as well as helping trainees to pass their examinations. The opening chapter is devoted to a concise outline of pathology and bacteriology, setting out the background to the processes of disease. Separate chapters are headed "Tuberculosis", "Venereal Disease", "Pain and Vomiting", "Acute Poisoning and Coma" and "Psychological Medicine"; then diseases of all the bodily systems are discussed under their appropriate headings. Perhaps one chapter which could be enlarged with benefit is that dealing with vitamin deficiencies. Descriptions of the actions of all the important drugs are clearly set out and a most useful table shows the approved or chemical name, the trade name and the diseases for which each is used; there is also an alphabetical list of the trade names which enables a cross-reference to be made to find out just what drug is contained in any pill or potion labelled with a name that often conveys no meaning.

Throughout there are many excellent illustrations, some of which are colour plates, and a series of cartoon-like drawings point out many pertinent features of prophylactic, pathological or therapeutic importance. Without the index, the work runs into 618 pages, from which it can readily be seen that it is of full text-book size, and nurses and their lecturers will find this book presents a very complete practical cover of modern medicine.

Fluoroscopy in Diagnostic Roentgenology. By Otto Deutschberger, M.D., with an Introduction by Frank J. Borrelli, M.D., F.A.C.R.; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 10" × 7", pp. 790, with 523 illustrations. Price: £11.

IT is claimed that this is the first complete volume to be published on fluoroscopy alone. The author describes the various types of apparatus used, including both fixed and tilting units, using a fixed tube with movable screen. He also describes a useful biplane fluoroscopic table which is of special value in locating foreign bodies in the lungs. He also refers to the great value of apparatus now available which uses the electronically produced image, which gives clear images that can be easily seen in an ordinary room without much visual adaptation.

The author advises the use of glasses about one dioptre greater than those usually used in the operator's reading glasses. Dark adaptation should take half an hour and in older people longer. Vitamin *A* accelerates adaptation. If red glasses are used a further time of about four minutes is needed in complete darkness. The author takes up rather too much space in detailing the advantages of the method. He considers that an operator becomes fatigued after two hours of screening and he limits his sittings to five stomach and twenty chest examinations. The author rather minimizes the dangers of fluoroscopy to patient and operator and fails to convince us that the method is as harmless as he claims it to be. The method is of great use in localizing foreign bodies in all regions. It is also of great help in chest work where films must also be taken for the detection of the smaller lesions.

Fluoroscopy's greatest field of usefulness is in the study of the digestive tract, and this section of the work can be studied with advantage by the most expert worker. The preliminary screening of the abdomen is of great value in cases of obstruction and frequently the site of obstruction can be decided.

Its use in cranial, urological and gynæcological work is very limited. In gall-bladder work its greatest use is in cholangiography. The author recommends röntgenography in the examination of the skeleton, but fluoroscopy is of value in the localization of foreign bodies and in the setting of fractures.

This work is a painstaking compilation and contains a wealth of useful information.

Practical Endocrinology. By Lewis M. Hurxthal, M.D., in cooperation with A. Seymour Parker, M.D., and Hirsh Sulkowitch, M.D.; *1955. New York: Landsberger Medical* Books, Incorporated. 8″ x 5½″, pp. 318, with 17 illustrations. Price: $7.00.

WITH the publication of this book, Dr. Hurxthal, who is Professor of Internal Medicine at the justly famous Lahey Clinic, Boston, goes far to fulfil a long-felt need. The book aims to deal with the clinical and therapeutic aspects of endocrinology, from a practitioner's point of view, and to do so without enlarging on obscure details, or digressing too far into the theoretical field. The result in the main is achieved with admirable clarity and brevity. A comprehensive review of endocrinology apart from diabetes is given. Very welcome additions are the chapters on hirsutism and endocrine disorders of infancy and childhood, subjects of ever-recurring importance to those in practice, and about which little has been written that is not in inaccessible treatises. Such a book could help dispel the ignorance and misconceptions of even those recently graduated in this subject: a twilight of knowledge which has for too long been illuminated often only by dazzling monographs. The book achieves more than its author's purpose and will be an important addition to the libraries of those concerned with clinical practice.

Diseases of the Liver and Biliary System. By Sheila Sherlock, M.D. (Edin.), F.R.C.P. (Lond.); 1955. Oxford: Blackwell Scientific Publications. 9″ x 5½″, pp. 734, with 198 illustrations. Price: 50s.

THIS book is a triumph for the author, for the Postgraduate Medical School of the University of London and for the publishers. Dr. Sherlock has made a comprehensive cover of the many diseases of the liver and one can select only a few for individual comment. She stresses the importance of diagnosis, paying particular attention to the value of a well-elicited history and bedside examination, followed by liver function tests designed in the main to differentiate between primary hepatocellular jaundice and jaundice due to external obstruction. As a pioneer of liver biopsy Dr. Sherlock gives good guidance regarding its value and limitations; she stresses its value in the diagnosis of nutritional hepatitis, diffuse malignant infiltration of the liver and hæmochromatosis, but gives a warning that in jaundice due to extrahepatic obstruction the cause is rarely shown by liver biopsy, and laparotomy should be performed. The section on virus hepatitis in its acute and chronic forms is full of wisdom. The author has included a fascinating section describing neonatal virus hepatitis; she states that "the disease may be a cause of stillbirth or the affected infant may die soon after birth, before jaundice has had time to develop. More clinically obvious is the type in which icterus of varying intensity is apparent during the first fortnight of life. Recovery may occur within a few weeks or the disease may last weeks, months or even years, during which time it passes through the stages of chronic hepatitis to frank cirrhosis".

Difficulty in the diagnosis of primary carcinoma of the biliary tree is recorded and the author is gloomy regarding the chance of giving surgical aid. It may well be that further studies may reveal that the surgeon can give increasing aid to patients suffering from this distressing condition, even though the relief from jaundice, pruritus and general debility may be only temporary.

Two major problems may confront the physician—the treatment of hepatic coma and œsophageal hæmorrhage, the two often being associated. In her discussion, Dr. Sherlock emphasizes the grave nature of these conditions and the need for a plan of action. In hepatic coma she discusses the value of glutamic acid to counter the ammonia retention, and in her experience the results have not been favourable. It may be observed, however, that more recent work by Walshe (*The Lancet*, 1955, 1: 1235) suggests that this form of therapy may still have a place in our plan especially in coma due to long-standing cirrhosis, whereas it is rarely of value in patients suffering from "massive hepatic necrosis", the latter most frequently being due to acute virus infection. With regard to massive and continued œsophageal bleeding, the various surgical procedures are enumerated and the successful use of balloon tamponage is described.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Object Relations Technique", by Herbert Phillipson, M.A.; 1955. London: Tavistock Publications, Limited. 8½″ x 5½″, pp. 232, with 12 illustrations. Price: 21s.

Deals with personality assessment. The author "attempts to show that personality dynamics in terms of object relations are reflected in the process of perception".

"Asclepiades, His Life and Writings: A Translation of Cocchi's Life of Asclepiades and Gumpert's Fragments of Asclepiades", by Robert Montraville, M.D.; *1955. Connecticut:* Elizabeth Licht, publisher. 9″ x 6″, pp. 178. Price: $6.00.

It is stated in the preface that this is the first book printed on Asclepiades since 1941.

"Psychological Medicine: A Short Introduction to Psychiatry", by Desmond Curran, M.B., F.R.C.P., D.P.M., and Maurice Partridge, M.A., D.M., D.P.M.; Fourth Edition; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 8½″ x 5½″, pp. 416, with 20 illustrations. Price: 21s.

The first edition appeared in 1943.

"La Lèpre", by Roland Chaussinand; 1955. Paris: Expansion Scientifique Française. 9″ x 7″, pp. 310, with 130 illustrations. Price: 3.800 fr.

The first edition was published in 1950; it has been completely revised and reset.

"Refresher Course for Practitioners: Specially Contributed Articles from the Journal of the Indian Medical Association", Volume I, edited by P. K. Guha; 1955. Calcutta: *Journal of the Indian Medical Association.* 7½″ x 4½″, pp. 380, with many illustrations. Price: Rs. 8.

There are 32 chapters contributed by "specialists eminent in their own fields".

"Studies on the Cerebral Cortex (Limbic Structures)", by Santiago Ramón y Cajal; translated from the Spanish by Lisbeth M. Kraft; 1955. London: Lloyd-Luke (Medical Books), Limited. 8½″ x 5½″, pp. 192, with 108 illustrations. Price: 27s. 6d.

This translation was made in celebration of the one hundredth anniversary of Ramón y Cajal's birth.

"Biochemistry for Medical Students", by William Veale Thorpe, M.A. (Cantab.), Ph.D. (Lond.); Sixth Edition; 1955. London: J. and A. Churchill, Limited. 8″ x 5½″, pp. 550, with 44 illustrations. Price: 27s. 6d.

The fifth edition appeared in 1952; the advances in the subject have made a new edition necessary.

The Medical Journal of Australia

SATURDAY, DECEMBER 24, 1955.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words of phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

CHRISTMAS AND THE BOOK OF PROVERBS.

The heart of the wise teacheth his mouth,
and addeth learning to his lips.
Pleasant words are as an honeycomb,
sweet to the soul and health to the bones.

PROVERBS xvi : 23 and 24.

He that is of a merry heart hath a continual feast.

Ibidem xv : 15.

WHEN peace on earth and goodwill to men were heralded on the first Christmas morning a seasonal attitude of man to his fellow was created which has lasted ever since. Christmas time has by common consent become a season of merry making, of feasting and light-hearted jollity, when the right hand of friendship is extended, when differences of opinion are set aside and when many a personal feud is forgotten. We have probably all seen grumpy men become cheerful under its influence, the taciturn become talkative and the grim lose their forbidding looks. Many of those, even, who do not recognize the origin of the feast cannot avoid its influence, and they enter into the Christmas spirit of friendship and the giving of gifts. For those whom Christmas passes by unheeded we can have nothing but pity.

To radiate peace and good-will (at Christmas or indeed at any time) a man must be at peace within himself; this means that he must have the kind of wisdom that is praised by Solomon. Solomon writes of a folly that "is joy to him that is destitute of wisdom"; but he also tells us to "go from the presence of a foolish man" when we perceive not in him "the lips of knowledge", for "the wisdom of the prudent is to understand his way, but the folly of fools is deceit". We know that the laughter of fools has been compared to the "crackling of thorns under a pot", and Solomon reminds us that "even a fool, when he holdeth his peace, is counted wise; and he that shutteth his lips is esteemed a man of understanding". Incidentally—and this has nothing to do with the joy of Christmas—it is true that a clinician in his consulting room, who is quite at a loss to understand his patient's problem, is often thought to be exceedingly wise if his expression is grave, if he knits his brows, if he nods his head slowly as one possibility chases another through his anxious mind, and if he says not a word. We need not consider further the pseudo-wisdom of silence, although it is true that "he that hath knowledge spareth his words". The wisdom at which we should aim is that which "resteth in the heart of him that hath understanding". Further—"he that is slow to wrath is of great understanding; but he that is hasty of spirit exalteth folly". Again: "A wrathful man stirreth up strife; but he that is slow to anger appeaseth strife." Most human action would be made clear if the motive was known: "A sound heart is the life of the flesh; but envy the rottenness of the bones." If the motive is self, either in professional or in social circles, it is salutary to remember that "before honour is humility". As we strive to attain wisdom, then, we shall put behind us envy and uncharitableness which are foreign to the Christmas spirit.

We know that "out of the abundance of the heart the mouth speaketh", and a wise man will speak pleasant words which "are as an honeycomb" and "sweet to the soul". Words of this kind are the words for Christmas. We know that a man who speaks from the abundance of his heart will not speak lying words. On the contrary his words will perhaps make those who differ from him search, deeply if necessary, to discover the abundance of his heart, no doubt to their edifying. Abundance in the heart is not dependent on abundance of wealth. Solomon reminds us that "he that is greedy of gain troubleth his own house", and he also writes: "Better is a little with righteousness than great revenues without right." In another place we read: "How much better is it to get wisdom than gold! and to get understanding rather to be chosen than silver."

Pleasant words, kindness and generosity of mind and of goods will make merry many a heart at Christmas time—and "a merry heart doeth good like a medicine". We have said that Christmas time is a time not only of merriment, but of feasting. Let us then have our feasts—plum puddings, meats and all, with the usual trappings and a little, but not too much, alcohol, if it is to our liking. But let us remember that behind all the jollification, all the giving of gifts, and all the delightful nonsense, all the make-believe in which some of us indulge, there is the merry heart. "Better is a dinner of herbs where love is, than a stalled ox and hatred therewith." Solomen tells us that "he that is of a merry heart hath a continual feast". When therefore we wish our friends a "merry Christmas", we wish them not only a happy reunion with their families and friends, but the merry heart which will promote peace and goodwill and be a continuous source of strength to them.

Current Comment.

POLIOMYELITIS.

THE World Health Organization has assembled in one volume a series of 14 articles on poliomyelitis written by some of the world's leading authorities.[1] There are five sections, covering epidemiology, clinical aspects, virology, immunology and control. The great advantage of this publication lies in the way in which each writer has collected, and incorporated with his own knowledge, all the latest worthwhile data on his section of the work, from the literature of the world; thus we are presented with an expert summary of each facet of the subject in a compact and organized form. In these circumstances it is difficult to pick out individual points for comment, especially as much of the information describes the present situation as it is, and offers no concrete conclusions. However, as regards epidemiology, J. R. Paul summarizes the situation as follows: where sanitation is primitive and living conditions are crowded, facilities for spread of the virus are good, and infants come into contact with it early in life; few reach the age of three years without having suffered at least an inapparent infection with one strain; no large group of susceptibles is built up, and the disease remains in a state of smouldering endemicity. Where sanitation and living conditions are good, large numbers of children reach the age of, say, ten years without having acquired any infection or immunity, and the ground is thus prepared for epidemics. In these circumstances, artificial immunization offers the most reasonable hope for control of the disease.

Debré and Thieffry, dealing with the clinical aspect, point out that paralytic poliomyelitis is a definite and characteristic disease easily capable of clinical diagnosis, whereas when non-paralytic fevers occur, their diagnosis as poliomyelitis is presumptive and not easily capable of proof. The articles on treatment, by W. R. Russell and H. C. A. Lassen, are up to date and complete. Much of the material in the section on virology is technical, but we learn that *Poliovirus* is one of the hardiest viruses known, which partly accounts for its wide dissemination and long persistence in suitable environments. A. B. Sabin's section on immunity and vaccination, while it states the situation regarding killed-virus and avirulent variant vaccines, was written before the Salk experiment, and contains no topical references to this important subject. The same applies to H. R. Koprowski's article. Taken as a whole, however, this publication is a most valuable survey of the subject, though about two years behind its title-page publication date; so that although its basic data are accurate, it would be necessary for anybody wishing to use it for advanced work to be able to add to it the most recent advances and to recognize the outdated portions of it.

In this last-mentioned respect attention is drawn to a series of papers[2] read in a panel discussion on "Prospects for the Control of Poliomyelitis" at the annual meeting of the American Medical Association in June, 1955. Jonas E. Salk describes his approach to the preparation and use of poliomyelitis virus vaccine. L. A. Scheele, Surgeon-General of the United States Public Health Service, and J. A. Shannon, Associate Director of the National Institute of Health, United States Public Health Service, consider the public health implications in a programme of vaccination against poliomyelitis; they refer to the much-publicized experience with the Cutter vaccine and to recently amended requirements for manufacture and safety testing of poliomyelitis vaccine aimed at the production of potent material that is safe. T. D. Dublin, medical consultant to the Vaccine Division, National Foundation for Infantile Paralysis, reports on the 1954 poliomyelitis vaccine field trial, its plan, field operations and follow-up observations, and Thomas Francis, junior, presents an evaluation of the trial. In addition to these four papers is a record of the discussion following their presentation and of the questions asked and answers given at the panel discussion. In the same journal is a second paper by L. A. Scheele on the control of poliomyelitis through vaccination, in which he presents some important aspects of the Public Health Service's point of view. It is obvious that more needs to be known about the whole question, but the publication of these papers will do a good deal to resolve confusion and to allay any impression given by the popular Press that the public health authorities in the United States are approaching the problem in anything but a responsible way.

[1] "Poliomyelitis"; World Health Organization: Monograph Series; 1955. Geneva: World Health Organization. 9½" × 6¼", pp. 408, with many illustrations. Price: £2.

[2] *J.A.M.A.*, August 6, 1955.

THE EFFECT OF RETROLENTAL FIBROPLASIA IN CHILDREN.

AN interesting study on the effect of retrolental fibroplasia in children has been performed by A. C. Krause in Chicago.[1] One hundred and seven children, born between the years 1937 and 1951, were studied so that ages varied from four to seventeen years. These children were investigated by pædiatricians, social workers, psychologists and psychiatrists. The children with retrolental fibroplasia born from 1937 to 1941 fared poorly; one-third died of disease unrelated to retrolental fibroplasia. Children born in the last ten years were less handicapped physically and mentally.

The range of corrected vision varied greatly from 20/30 to nil. Fixation nystagmus, high optical correction, and mental retardation decreased vision. In a few children binocular vision was much higher than vision in either eye. About 60% of the children had a myopia over five dioptres and 40% a myopia of over ten dioptres. The adjustment of the children to school was poor in the older children; the eight to twelve years group showed much better physical and mental development. If possible they were kept with sighted children of the same age group. When the child was isolated the tendency was towards general retardation. The four to seven year olds had the highest educational recovery value. In most children vision was bad, refraction was performed early and where errors were high glasses were ordered after the age of eight months, especially in myopes. The refractions were repeated annually. It was found that vision was not always static.

Education of these children is a major problem. In the severe forms of blindness the child tends to have an environment of over-protection or rejection. Stimulation and companionship of the other children are the main factors in preparation of the child for school. The aim is to send the child to a sighted nursery school where the experience of being with sighted children and being accepted by them is important for later life and helps to overcome mannerisms and emotional patterns of the blind child. Some children were retarded physically and mentally. However, some of these children have a recovery value and Krause urges that they should not be placed in institutions for mentally retarded children until it is certain that the condition is unchangeable.

[1] *Arch. Ophth.*, April, 1955.

INTESTINAL ABSORPTION OF FAT.

THERE is still much controversy as to how fats are absorbed from the intestinal tract and what is the origin of fæcal fat. In an attempt to elucidate one part of the problem R. Blomstrand[2] has studied the intestinal absorption, using isotopic carbon labelled oleic and palmitic acids. In an earlier study, using the same methods, he found that normal infants absorb about 85% of fed labelled oleic acid. Most of the fæcal fatty acids of normal children

[2] *Acta med. scandinav.*, 1955, Volume 152, Number 2.

were dietary fatty acids. In the steatorrhœa of congenital biliary atresia and cystic fibrosis of the pancreas the amount of fed labelled fatty acids absorbed was 42% and 26% respectively.

In the present study two normal adult males and a patient with non-tropical sprue were investigated. The subjects were given a fixed diet containing 2·7 grammes of fatty acids in the entire daily food. The investigation extended over nine days. During the first and last three days 40 grammes of normal olive oil were given daily and during the middle three days 40 grammes of olive oil containing oleic acid or oleic and palmitic acids labelled with ^{13}C. The pooled fæces for each day were analysed for total lipids, total fatty acids, unsaponifiable material, isotopic concentration of the total fatty acids, and proportion of saturated and unsaturated fatty acids. Of the labelled fatty acids fed 99·4% was absorbed in each normal subject. If the percentage of absorption had been calculated according to ordinary balance technique the percentage of absorption would have been about 94%. The non-dietary fatty acid excretion makes the difference. During periods II and III the average daily excretion of fatty acids by the normal subjects was 1·2 grammes and 1·1 grammes respectively. The non-dietary fat excreted was calculated as about 1·0 gramme, so fat fed supplied very little of the fatty acids excreted. The excreted fat probably came mainly from desquamated intestinal epithelial cells and bacterial synthesis of fatty acids. In the patient with non-tropical sprue 76·5% of the administered labelled fatty acids was absorbed. There was thus a great impairment in fat absorption and the figure obtained is much the same as that obtained by other workers using different techniques. The unabsorbed labelled fatty acids then formed a major part of the excreted fatty acids. There was, however, about three times as much non-dietary fatty acid in the fæces as in normal subjects, probably because of increased desquamation of intestinal mucosa.

MYO-ELECTRIC CURRENTS TO OPERATE PROSTHESES.

AFTER amputation the motor patterns for movements of the lost parts remain intact, and the remaining intact muscles, on receiving impulses to make movements, contract and set up myo-electric currents. These facts have been taken advantage of by C. R. Battye, A. Nightingale and J. Whillis[1] in their construction of a prosthesis directly controlled by the wearer's cerebral cortex and requiring no reeducation of muscles. The apparatus consists first of a pair of electrodes, chlorided silver cups held to the skin by collodion. By numerous experiments it was found that in either grasping with the whole hand or pinching between the finger and thumb, the *flexor pollicis longus* was the most satisfactory prime mover, and the *brachioradialis* was the most satisfactory synergist if the *flexor pollicis longus* was not available. By trial and error with each individual patient the best sites for placing the electrodes to secure the maximum strength of the myo-electric current and the minimum interference from adjoining muscles were determined. The leads from the electrodes are taken to a balanced amplifier, which cuts out main variations, and by being limited to a narrow frequency range, reduces random fluctuations within the system itself. Thereafter the amplified impulse passes through a discriminator to a solenoid, which, when switched on, closes a split hook on the prosthesis. Thus the impulse to close the hand, initiated in the cerebral cortex, is immediately transmitted to a closing action of the split hook.

This apparatus has possibilities for use at the work-bench or the meal table, but it is cumbersome and expensive in the pilot design so far produced. Nevertheless, since the principle has been established and its practical application proved, there is no doubt that modern engineering could produce a lighter and more precise piece of apparatus, capable of being transported easily and of being plugged into any ordinary source of electric power. In fact, the possibilities which this preliminary work has opened up are very extensive.

[1] *J. Bone & Joint Surg.*, August, 1955.

RH SENSITIVITY AND SALK VACCINE.

BECAUSE the Salk vaccine is grown in cultures of monkey tissue, and often of monkey red cells as well, the question arose of the possibility that injections of the vaccine might cause sensitization to Rh antigens in Rh-negative girls, or to other blood factors in Rh-positive persons. Theoretically, such sensitization was regarded as impossible, but as Neva M. Abelson, R. M. McAllister, A. Greene and L. L. Coriell[1] point out, it is not justifiable to discuss on theoretical grounds a question which is capable of being answered experimentally; accordingly these workers carried out a series of experiments. That, by testing paired sera collected before and after vaccination from Rh-negative children, no development of Rh antibodies can be found is not conclusive, since injection of Rh antigen does not necessarily provoke an immediate response, but may occasionally promote *erythroblastosis fœtalis* during a subsequent pregnancy with an Rh-positive fœtus. However, when Rh antigen is injected into an isoimmunized person there will be a measurable antibody response, and these workers collected three groups of eight sensitized volunteers; each group was given Salk vaccine produced by different manufacturers. In two groups there was no rise in antibody titre; in the third group, consisting of persons quite recently sensitized, there was a small rise, which was considered to be anamnestic in nature; this was confirmed when the same vaccine was later given to the other two groups without producing any antibody increase. Furthermore, when Rh-negative persons who were not previously sensitized were given potentially sensitizing injections of vaccine, and were later tested with Rh antibodies, no sensitization was found to have occurred. The authors conclude that these experiments indicate that the theoretical impossibility of Salk vaccines causing Rh sensitization is given complete practical confirmation. Since the original question was admittedly a reasonable one, it is most satisfactory to have it definitely answered in this way.

[1] *J.A.M.A.*, September 24, 1955.

THE EFFECTS OF COLD ON SWIMMERS.

MUCH research on the part played by cold on persons immersed in the sea has recently been carried out by the defence services of various countries, but the details have not been made public. Under ordinary circumstances it is accepted that after shipwreck, for example, the average time of survival in the sea at a temperature of 60° F. is five to six hours. Yet in 1951, 20 competitors entered the race across the English Channel, and 18 completed the course in from twelve to twenty hours in water at a temperature of 60° F. This fact prompted L. G. C. Pugh and O. G. Edholm[2] to investigate the physiology of long-distance swimmers. They made observations on swimmers in Lake Windermere, and on 16 competitors in the 1954 Channel race. Their conclusions were that some persons tolerate hypothermia better than others, apparently because their power to maintain their body-temperature is better; body-temperature falls only when the swimmer becomes fatigued and his expenditure of energy decreases, whereupon a kind of hypothermic muscular weakness supervenes, presumably setting up a vicious circle. Furthermore, the heat production of Channel swimmers is not exceptionally high, but that it can be kept up for so

[2] *Lancet*, October 8, 1955.

long as twenty hours is remarkable—presumably training is the important factor here. But the main feature is body fat. The fatter the swimmer, the better his insulation and the less his rate of heat loss; most persons, even when immersed in cold water and keeping still, do not lose heat very rapidly, but fat persons lose less while swimming than while keeping still, while thin persons lose more while swimming. This apparently paradoxical effect is probably influenced in part, however, by the training factor, by reason of which the trained person can utilize his energy more efficiently and for a longer time than the untrained; but if there is increased heat production, the better insulated person has the advantage. The smearing of grease on the body appears to have little effect on heat loss. Arising from these experiments and observations is the suggestion that shipwrecked persons would have the best chances of survival if they clung to pieces of wreckage and did not struggle or swim about; and that if anybody has to do much swimming, the fattest should undertake it.

THE DIAGNOSIS OF SUBACUTE BACTERIAL ENDOCARDITIS.

THE effectiveness of present-day treatment of subacute bacterial endocarditis has increased the practical importance of early diagnosis of the disease. Unfortunately, it is still sometimes missed, and so the opportunity for giving life-saving treatment may be lost. The classical signs and symptoms of subacute bacterial endocarditis are well known and need not be reiterated. Moreover, they are present in the majority of cases; so that the clinician of reasonable experience will usually light on the correct diagnosis. The real problem, which may be a matter of life and death to the patient, arises when characteristic clinical features are absent. Attention is drawn to this in two recent articles,[1] one analysing a series of cases in patients of all ages, the other putting forward some important but little appreciated aspects of the problem of diagnosis as it relates to elderly patients. John Wedgwood, from Addenbrooke's Hospital, Cambridge, has examined the records of 65 patients with subacute bacterial endocarditis, with an age range from childhood to over seventy years. In every case the diagnosis was confirmed either at post-mortem examination or by culture of organisms from the blood during life. The clinical features varied from case to case, but two were almost always present during the first week after the patient's admission to hospital: a heart murmur was present in 63 of the 65 cases and pyrexia in 60. The incidence of other features (embolism, Osler's nodes, petechiæ, *café-au-lait* complexion, clubbing of fingers, palpable spleen) lagged a good way behind, and it is notable that in 13 cases heart murmur and pyrexia were the only classical signs present in the first week after the patient's admission to hospital. Wedgwood states that the most common cause of delay in diagnosis was the similarity of the symptoms of subacute bacterial endocarditis to those of everyday illnesses; hence a diagnosis of "flu" or the like was easily made. Subacute bacterial endocarditis will be detected in its early stages only if its possibility is constantly borne in mind. Of symptoms which should excite suspicion, persistent pyrexia or ill-health is the most important; others are recurrent attacks of "flu", persistent loss of weight, anæmia, attacks of fibrositis or of pain, rheumatic fever not responding to salicylates, hæmaturia, recurrent attacks of pleurisy from pulmonary embolism, and cerebral embolism. These are, of course, by no means specific clinical features, but the accompanying sign that indicates their likely association with subacute bacterial endocarditis is a heart murmur, which is usually loud and obviously associated with valvular disease. Other helps in diagnosis can usually be found from a carefully elicited history and a thorough physical examination, but the fundamental signs remain pyrexia and a heart murmur. Confirmation depends on the culture of organisms from the blood, which may need to be repeated, and perhaps on the exclusion of other diseases. Trial therapy with penicillin may be a later court of appeal.

In the elderly subject diagnosis may be particularly elusive, and it is possible that for this reason the rarity of the condition in older people is more apparent than real. H. J. Anderson and J. S. Staffurth examined the records of 76 patients treated for subacute bacterial endocarditis at Saint Thomas's Hospital, London, between 1946 and 1954, and found that 14 (nearly one-fifth of the total) were over the age of sixty years, including five over the age of seventy years. This proportion is greater than any that they have been able to find previously reported, and their figures, taken in conjunction with some Registrar-General's figures for deaths from subacute bacterial endocarditis after the age of sixty years, suggest that the diagnosis is missed because of lack of awareness of its occurrence in this higher age group, and that some of these elderly subjects die with their condition undiagnosed. Examination of the case histories in Anderson and Staffurth's series indicates that, although in many respects subacute bacterial endocarditis in the elderly is similar to that in younger subjects, several features may be different and are worth emphasizing. In some cases the disease is in every way similar, the onset being relatively definite, and in two cases of the series it followed tooth extraction. The presence of pyrexia, clubbing of fingers and a palpable spleen, in conjunction with a heart murmur, soon leads to blood culture and the correct diagnosis. Evidence of emboli, however, apart from a few petechiæ, was rare in this series. In other cases the onset is much more insidious: fever and a heart murmur may be the only signs; and if the presence of a murmur is accepted as a common and often insignificant finding in the elderly, the diagnosis will be long delayed.

It is notable that these two papers, prepared in two quite separate centres and approaching the question from different points, bring the same main conclusions into focus: early diagnosis of subacute bacterial endocarditis is of vital importance; the clinician must maintain an awareness of the condition in the presence of a vague illness, even in elderly subjects; pyrexia and a heart murmur are practically constant features, sometimes they are the only characteristic features, and the combination should never be treated lightly; blood culture should never be neglected, but negative findings, even if repeated, do not exclude the diagnosis, which may be confirmed by a therapeutic test.

[1] *Lancet*, November 19, 1955.

EARLY ORTHODONTIC TREATMENT IN CLEFT PALATE CHILDREN.

WHEN should orthodontic treatment be started for the cleft palate patient? It should be started early. It was once proposed when all the permanent teeth had erupted, that was the time to begin orthodontic treatment. The application of this principle in the cleft palate patient or in anyone requiring orthodontic care should be recognised as a gross injustice to the child with the deformity. *The majority of orthodontists today do not realise this fact, that orthodontic therapy must be started at four years of age. When the permanent dentition is complete it is too late to move and mold the maxillæ.*

This statement appeared in *Plastic and Reconstructive Surgery*, July, 1955, in an article by George Warren Price, D. F. Terwilliger, Vincent Pennisi, junior, and E. Horace Klabunde. The italics are the authors'. Seventeen years of experience with early orthodontic therapy in cleft palate cases has convinced the authors that this treatment should be instituted at four years of age, or as soon as the child becomes cooperative. Contrary to general opinion, that tooth movement takes place only within the bone, the authors have shown that soft bone itself can be moved and shaped early and that growth direction can be changed. Early orthodontic therapy in cleft palate children has a threefold physiological effect: the mass movement of the maxillæ and their component parts, a bending of the alveolar processes and finally tooth movement. The basis of orthodontic therapy today is in the fact that the teeth

may be moved by the application of gentle forces over long periods of time. The changes that occur in the alveolar bone are primarily bone resorption and new bone formation. The tension of pull produces bone deposition while the portion of alveolus receiving the pressure becomes resorbed. Therefore, movement is permitted without significant trauma to the periodontal membrane.

Between the ages of three and five years with the proper approach, orthodontic therapy may be started. It is during this time that tooth movement will exert its most favourable or unfavourable results. In the bilateral cleft with the premaxilla almost locked out of the dental arch by the wedging attacks of the right and left alveolar processes, it is most essential to commence early orthodontic care. The right and left alveolar processes and the lateral palatine processes can be moved laterally at this time to permit adequate space for admittance of the premaxilla, a normal dental arch being thereby established. Early orthodontic care becomes an important adjunct to achieve the maximum of good speech and also will remove much of the oro-facial stigma that these children and adults must bear.

The authors have established a Cleft Palate Guidance Group for long-range planning and rehabilitation, and this article is based on work which has been done within this group. The plan of management is outlined and cases are presented. Not quite twelve months ago, a similar Cleft Palate Clinic was formed at the Royal Alexandra Hospital for Children, Sydney, and it comprises a group of surgeons, orthodontists, speech therapists and oto-rhino-laryngologists. This group has met regularly and has reviewed old cases and examined new patients. The object of the clinic is to gain experience in all aspects of the treatment of cleft lip and cleft palate and to ensure that sound integration of all component parts of therapy, surgery, orthodontia, speech training *et cetera* is ensured, at the proper time. Already, the surgeons themselves have gained considerably in their association with the ear, nose and throat surgeon, from the pædodontist, from the speech therapist and from other members of the clinic. It is not anticipated that this clinic will be in a position to produce a statement of its work for some years because, to be of any value, such a statement must be based on a reasonable number of well-studied cases. However, the group feels that its study must ultimately reflect improvement on the treatment and rehabilitation of cleft lip and cleft palate patients.

LOCAL ANÆSTHETICS IN THE TREATMENT OF EPILEPSY.

VERY little work has been done on the effects of local anæsthetics on the central nervous system, probably because several central functions—for example, the spinal reflexes and transmission in the ascending system connected to low threshold afferent fibres—are very little affected by intravenous injections of local anæsthetic agents in moderate doses. C. G. Bernhard and E. Bohm have shown that some of these drugs have a pronounced blocking effect on the post-stimulatory epileptiform cortical after-discharge.[1] Repetitive cortical stimulation was given to the exposed brains of cats and monkeys, and records were made of the epileptiform cortical after-discharge. These discharges were largely or completely prevented by the intravenous injection of certain local anæsthetics. Different intravenous doses of procaine, butethamine (iso-butylaminoethyl p-aminobenzoate), lidocaine (diethylaminoacetate-2:6-xylidide, xylocaine, lignocain A.N.), diethoxine (di-ethylaminoethyl-4-ethoxybenzoate hydrochloride) and tetracaine (2-dimethylaminoethanol 4-n-butylaminobenzoate hydrochloride, amethocaine) were tested. Lidocaine was more effective than procaine and butethamine, while diethoxine had about the same potency as lidocaine. Tetracaine was the most efficient, but is relatively highly toxic. Lidocaine seemed to be the most useful for therapeutic use, as its toxicity is low.

[1] *Brit. J. Pharm. & Chemotherapy*, September, 1955.

The facilitatory effect on the motor neuron built up by cortical stimulation, which persists after the cessation of the repetitive cortical stimulation, is abolished by lidocaine in parallel with the abolishment of the cortical after-discharge. Barbiturates have some effect in reducing the duration of the cortical after-discharge, but, even in large doses, do not abolish it. On the other hand, small doses of pentobarbitone increase the sensitivity of the cortical after-discharge to lidocaine, but this effect reaches a maximum after quite small doses of pentobarbitone. A small dose of lidocaine with a small dose of phenobarbitone can bring about total abolition of the after-discharge.

These results have been confirmed in investigations in man. The conclusion is that the combination of a small dose of a barbiturate with a moderate dose of lidocaine is the most effective treatment for the temporary abolition of severe epileptic fits. The addition of the barbiturate to the lidocaine prevents the excitatory effects of lidocaine, which have sometimes been observed in man after the intravenous injection of lidocaine. This is a very interesting and entirely new approach to the task of controlling severe epileptic fits in man, and further observations will be welcome.

SURGERY OF THE HEART AND GREAT VESSELS.

THE notable part played by British medicine and surgery in the development of the surgical treatment of diseases of the heart and great vessels is clear from the issue of the *British Medical Bulletin* for September, 1955, which is devoted to a symposium on the subject. This is a subject on which the medical profession in general should be kept informed, even though its highly specialized detail concerns only the elect. As Sir Russell Brock points out in an introduction to the symposium, the subject is a recent and very rapid development, and it has attracted so much interest, often of a sensational nature, that it is in danger of being wrongly appraised. "To many it is still a desperate form of therapy and, because new, still uncertain and untried." However, the results are not necessarily uncertain. Experience is now extensive, and a notable degree of success has been achieved. Brock cites the surgery of mitral stenosis, which a few years ago was one of the great unsolved problems of surgery; now it has brought relief of disability to thousands throughout the world and saved the lives of many who otherwise had no hope when routine medical treatment had failed. In some other sections of the surgery of the heart and great vessels success has been less striking and difficulties have been greater, but in all some progress has been made. In this *Bulletin* 17 articles, all by leaders in their own fields, cover the important ground. They deal in turn with the surgical treatment of cyanotic heart disease (mainly variants of Fallot's tetralogy), pulmonary stenosis, septal defects, coarctation, persistent *ductus arteriosus*, mitral stenosis, disease of the aortic valve and valvular incompetence. The physicians discuss the selection of patients for surgery, first, in congenital heart disease and, second, in acquired heart disease. Other articles are concerned with problems of anæsthesia, the role and technique of hypothermia, cardiac resuscitation, cross-circulation, and the artificial heart-lung and its practical application to cardiac surgery. A first-hand account is given of arterial reconstruction, special reference being made to the use of homografts. All the contributors write from first-hand experience. The result is illuminating and in a great measure reassuring. A striking change has come over a scene that until quite recently held little hope. This has been made possible by brilliant and painstaking work and by the sharing of ideas by surgeons, cardiologists, anæsthetists and others in many parts of the world. Britain's contribution has been outstanding and compares favourably with the extensive and brilliant work done in North America. At the same time we would point out the fallacy of assuming that for Australian sufferers from cardiac disability hope lies only over the seas.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Divergence Insufficiency.

D. J. LYLE (*Arch. Ophth.*, December, 1954) discusses divergence insufficiency, a condition which appears to be on the increase. The patient with divergence insufficiency complains of double vision for distance, with no diplopia for near. Recent trauma or infection is a most frequent cause. Vascular lesions produce the condition in the aged; tumours either by direct destruction or with secondary compression are also a cause. Multiple sclerosis, syphilis, diphtheria, chorea, lead poisoning, alcohol and other toxic agents have been cited as causes of divergence insufficiency. Deviation of the eyes is not evident on casual inspection and requires examination by tests of muscular action. In the differential diagnosis, the following must be eliminated: spasms of convergence, abducens paralysis, encephalitis with extraocular or intraocular muscular incoordination, dissociation of eye movements, *myasthenia gravis*, thyrotoxic ophthalmoplegia and various types of myopathies. Prisms base out relieve symptoms; but if the condition persists, operation on both lateral rectus muscles may be considered.

Unilateral Blindness Occurring During Anæsthesia for Neurosurgical Operations.

R. W. HOLLENHORST *et alii* (*Arch. Ophth.*, December, 1954) report eight cases in which unilateral blindness followed neurosurgical operation. Each patient complained of blindness in one eye immediately on regaining consciousness. Each had a dilated pupil which failed to react to the direct light reflex. The cornea was hazy, and the lids were œdematous. Examination of the fundus showed normal or dilated retinal arterioles, engorgement of the venules, and œdema of the macula and of the retina around the disk. The more severely involved eyes had a cherry-red spot at the macula. The authors consider that inadvertent pressure on the ocular structures and possibly lowered blood pressure in the orbital arteries are the cause of this condition.

Chelation of Calcium with Edathamil Calcium-Disodium in Band Keratopathy and Corneal Calcium Affections.

G. BREININ AND A. G. DEVOE (*Arch. Ophth.*, December, 1954) report on the use of edathamil calcium disodium (EDTA) in cleaning calcium from corneas showing band keratopathy. They consider that it should be the primary treatment for band keratopathy and may make corneal surgery unnecessary. The procedure is simple, and the patient need not be hospitalized. The cornea is cocainized, and then all the epithelium is removed. EDTA is applied in appropriate strength, 0·01M in light infiltrations and 0·05M in dense infiltrations. The solution should be warm, and is applied to the cornea by means of an iontophoresis cup. On completion of application an antibiotic ointment is instilled and the eye bandaged.

Treatment of Retinoblastoma by Irradiation and Triethylene Melamine.

A. REESE *et alii* (*Arch. Ophth.*, April, 1955) have been treating retinoblastoma by irradiation since 1936. The complication which has given greatest concern has been late vitreous hæmorrhage from retinal blood vessels presumably damaged by irradiation. In an endeavour to prevent or reduce the incidence of this hæmorrhage the authors have reduced the amount of irradiation to the lowest dose which would be lethal for the tumour. In an endeavour to use the lowest possible amount of irradiation and at the same time to be sure of destroying the tumour, it was decided to combine irradiation with the use of TEM (triethylene melamine), a drug which is given orally—a great advantage in children. In 1953 the authors treated retinoblastoma in the only eye where useful vision could be expected with irradiation and TEM. The tumour dosage was 3400*r*, which is about half the dose given without TEM. The dosage of TEM was 2·5 milligrammes for children under twelve months of age, 3·0 milligrammes for children aged twelve to eighteen months, and 3·5 milligrammes for older children. Blood and platelet counts were performed every two weeks. The total dose was usually 15·0 milligrammes in five divided doses. More recently the authors have been studying the effect of a single dose of TEM given intraarterially. They stress the point that alone TEM is valueless—its value lies in its synergistic action with irradiation.

The Effect of Phenylbutazone on Ocular Inflammation.

N. YOURISH *et alii* (*Arch. Ophth.*, February, 1955) undertook an experimental study to determine whether phenylbutazone was able to block ocular inflammation resulting from injection of glycerin into the anterior chamber of the rabbit's eye. They state that phenylbutazone is a synthetic drug introduced for the treatment of rheumatoid arthritis; it has therapeutic effects in some ways similar to cortisone, and, like cortisone, induces sodium retention and œdema. They found that the intramuscular injection of phenylbutazone blocked almost completely the inflammation induced by the injection of glycerin into the anterior chamber of the rabbit. In view of this it would seem worthwhile to try this drug in man in certain inflammatory conditions of the eye.

Angle Closure Glaucoma.

P. A. CHANDLER AND R. R. TROTTER (*Arch. Ophth.*, March, 1955) describe the differences between wide or open angle glaucoma and narrow angle or angle closure glaucoma, and consider more fully the pathology of angle closure glaucoma and its treatment. They state that in subacute angle closure glaucoma the angle is narrow and under the influence of various factors a portion of the angle closes and the tension rises. As a result of repeated and prolonged episodes of angle closure, peripheral synechiæ form. In most cases there is a history of periodic attacks characterized by ocular discomfort, blurred vision and seeing coloured haloes around lights. The eye is usually white. The anterior chamber is shallow, but more shallow in the periphery. The pupil is slightly dilated if the tension is elevated. The disk may be normal or show more or less cupping and atrophy. The tension may be normal. The visual field may be normal or show more or less glaucomatous defects depending on the degree of cupping and atrophy. Certain provocative tests may be of assistance in diagnosis, such as the moving picture test, darkroom test, mydriasis test and reading in a dim light. Medical treatment consists of using the usual miotics. Surgical treatment in early cases—that is, those in which there is a good response to miotics—is peripheral iridectomy; this cures the disease, or if there is any residual glaucoma, it can be controlled with miotics. If the disease is far advanced, a filtering operation is necessary.

Paraffin Method of Embedding Ocular Specimens for Microscopic Study.

D. WEXLER AND S. RICHARDSON (*Arch. Ophth.*, March, 1955) compare the celloidin and paraffin methods of embedding ocular tissues. In their own laboratory they have discarded celloidin and are using paraffin exclusively. Apart from the technical advantages is the fact that an eye processed in paraffin is available for study in seventeen days, as against about two months required for celloidin fixation. The authors describe in detail their paraffin-embedding technique.

Treatment of Herpes Zoster Ophthalmicus.

H. G. SCHEIE AND M. C. ALPER (*Arch. Ophth.*, January, 1955) report favourably on the use of cortisone and corticotropin in the treatment of *herpes zoster ophthalmicus*. In all cases except one the relief of pain was dramatic, pain nearly always disappearing within twenty-four to thirty-six hours. In all cases there were signs of irido-cyclitis either alone or accompanied by keratitis. Most patients received 20 milligrammes of corticotropin daily by intravenous injection, while atropine and cortisone were instilled into the affected eye. Antibiotics were usually given simultaneously to diminish or prevent secondary infection. The authors state that the hormones probably in some way block the response of tissues to the viral agent.

Uses and Abuses of Adrenal Steroids and Corticotropin.

M. HOGAN *et alii* (*Arch. Ophth.*, February, 1955) briefly describe the characteristics of each of the hormones used in ophthalmology and discuss their correct and incorrect therapeutic use. They state that cortisone may be given orally or by the intramuscular route; in most ophthalmic diseases 300 milligrammes are given on the first day, 200 milligrammes on the second day, and 100 milligrammes each day thereafter. In topical therapy solutions in strength 0·5% or 2·5% are administered as drops or by subconjunctival injection. Cortisone

acetate ointment (1·5%) is also used locally. Hydrocortisone has the same action as cortisone. Given orally the daily dosage is initially 80 milligrammes in divided doses, and the dose is reduced on succeeding days. It is used locally as drops or ointment in the same strength as cortisone. Corticotropin is given intramuscularly, 80 to 120 milligrammes per day in four doses at six-hourly intervals, and the dose is reduced to 50 to 80 milligrammes per day. For intravenous therapy 25 milligrammes of corticotropin may be dissolved in one litre of glucose saline solution and given as an intravenous drip over eight hours. The authors found that hydrocortisone was superior to cortisone for contact dermatitis of the lids, vernal conjunctivitis, sclerosing keratitis, superficial punctate keratitis, recurrent corneal erosions and diffuse episcleritis. An increased incidence of dendritic ulcers of the cornea has been found in patients treated for other conditions with local steroid therapy. There was an increase also of acute disciform keratitis, with necrosis, ulceration and perforation. Oral and parental therapy should be reserved for acute chorio-retinal inflammations adjacent to a vital area in the retina near the macula, papillo-macular bundle or disk.

OTO-RHINO-LARYNGOLOGY.

Soft Ear Insert.

J. P. ALBRITE (*Arch. Otolaryng.*, February, 1955) states that a soft ear insert has certain inherent advantages over the hard acrylic ear insert. The soft insert is more comfortable to wear, and with it there is no danger of injury to the external canal or tympanic structures in the event of a fall or a blow on the ear. Patients with extensive operations involving the external auditory canal can be properly fitted with ear inserts. The acoustic seal between the walls of the external ear canal and the insert is such that no acoustic feedback occurs; this eliminates interference with speech reception. Soft inserts might readily take the place of head set receivers now being used in radio communication and should be more comfortable. The soft ear insert is made of plasticized polyvinyl chloride. Of 1300 soft inserts issued at a United States army hospital, only one case was reported in which the patient was allergic to polyvinyl chloride.

Repair of Tympanic Membrane Perforations.

W. J. SCHRIMPF (*Ann. Otol., Rhin. & Laryng.*, March, 1954) states that the tympanic membrane must be intact in order to have a functionally perfect acoustic organ. Any perforation or loss of substance must result in some impairment of normal function. Various materials have been employed either to close over a tympanic perforation temporarily, or to act as a splint under which healing may be expected to take place. Amongst these, cigarette paper, waxed paper, "Cellophane", gold leaf and prepared sheep's mesentery have been employed. Several substances have been applied in an endeavour to freshen the margins of the perforation and to stimulate reparative processes. Silver nitrate, trichloracetic acid and "Euthymol" have each been of some effect. Human amniotic membrane is thin, transparent, tough and elastic. In addition the mesodermic chorionic side of the amnion adheres quite tenaciously to almost anything which it comes into contact with. The author prepares human amniotic membrane in the following manner. Several large clear pieces are cut free from the placenta and are placed in sterile sealed brown glass jars containing Ringer's solution with merthiolate one part per thousand of solution. Sterilization has been found after twenty-four hours and has remained for as long as four weeks. In all following steps the membrane must be handled aseptically. The membranes are first stretched out on a sterile towel to absorb most of the solution. Next the chorion is separated from the amnion by stripping with sterile forceps and scraping with a dull all-metal table knife. The side to which the chorion was adherent must be noted, as this is the adherent mesodermic side which will be applied against the tympanic membrane. The amnion is then cut into circular pieces such as will fit into a selected Petri dish, which is fitted with a piece of corrugated cardboard thoroughly impregnated with paraffin; this has all been sterilized in an autoclave. A piece of the damp amniotic membrane is next stretched, with the fœtal side downwards, over the paraffined cardboard and fixed with pins. The cardboard and stretched membrane, together with a small waxed container of calcium chloride to absorb moisture, is then placed within the Petri dish and covered over. This is allowed to dry for forty-eight hours or longer. Transfer may be made to another similarly treated Petri dish if drying is incomplete or should drops of moisture form inside. After the membrane is thoroughly dried, it presents a thin transparent appearance somewhat like "Cellophane" and is easily handled. With a metal punch pieces of various sizes are cut out, and these are stored ectodermal side up on a square of sterile waxed paper, which is then folded over as a pharmacist puts up powders. The packages are stored in a sterile Petri dish until needed. To apply the pieces to a perforation, the margins are first touched with 50% trichloracetic acid solution, and then a piece of amniotic membrane is applied mesodermal surface downwards against the perforation to cover it completely. Closure was successful in 48 of 53 cases treated. Improved hearing was usually obtained, the average gain in all frequencies in the air conduction audiogram being 18 decibels.

Œsophagitis and Stricture from Regurgitation.

L. R. CRANMER (*Arch. Otolaryng.*, June, 1955) states that œsophageal pathology has arely received the attention it deserves. The symptoms produced by œsophageal disease have frequently been attributed to cardiac, pulmonary, gastric and gall-bladder disease. Irritative inflammatory changes in the œsophagus, produced by the reflux of acid-peptic gastric contents, are probably much commoner than is realized. An incompetent cardiac sphincter and frequent association with hiatus hernia have been described. There may be a reflex spasm of the lower part of the œsophagus. Convincing cadaver and animal observations have demonstrated a causal relationship between the presence of acid-peptic contents in the œsophagus and œsophagitis and stricture. Apparently hydrochloric acid alone is not nearly so destructive as acid-peptic gastric secretions. Bile or pancreatic secretion mitigates the effect. Vomiting from various causes, including that of pregnancy, and the passage of a stomach tube have been cited as exciting causes, along with gastric ulceration and cholecystitis. The abnormality is typically present in the lower third of the œsophagus. As the disease progresses, ulcerations develop. Later, cicatricial stenosis occurs. Obstruction may cause stagnation of secretions and food, with bacterial inflammatory œsophagitis. Malnutrition, emaciation, spontaneous rupture and occasionally malignant degeneration may occur. The symptoms are few—dysphagia, hæmatemesis and retrosternal burning pain. There may be acid eructations and the tasting of food long after ingestion. The diagnosis is confirmed by X-ray and œsophagoscopic examinations, although these may have to be repeated before finality is reached. Biopsies may be necessary to exclude carcinoma. The treatment is aimed primarily at keeping gastric juice out of the œsophagus. Primary factors such as peptic ulcer, gall-bladder disease and metabolic and central nervous disorders may have to be overcome. Antacids and some of the newer antinausea drugs, such as dimenhydrinate, may be useful. If stenosis occurs, dilatation may be necessary. Surgery may be indicated when conservative measures fail.

Treatment of Tic Douloureux.

A. L. ROWLAND (*Arch. Otolaryng.*, May, 1955) states that the great auricular nerve is entirely a sensory nerve and is seen on dissection to send out innumerable fine terminal ramifications to the entire region, which is also innervated by the sensory supply of the trigeminal and facial nerves. It is a very much simpler and less hazardous procedure to approach and operate on the great auricular nerve than it is to reach and operate upon the trigeminal ganglion. One need merely incise the skin at the level of the junction of the upper two-thirds with the lower third of the sterno-mastoid muscle to come upon the nerve at the posterior border of the muscle. It may be possible at this level to detect a point of acute tenderness, and into this site an injection of 2% procaine solution may be made on to the deep fascia at a depth of about one-quarter of an inch. Usually two millilitres of the solution will suffice to infiltrate around the site. Absolute alcohol, 0·5 to 1·0 millilitre, may be subsequently employed in like manner. If desired, an inch or two of the nerve may be excised through an incision which exposes the nerve as it emerges at the posterior border of the muscle and turns to lie on the lateral aspect. Relief from superficial and deep sensations of pain in the face was notable in a patient who underwent this operation.

Clinico-Pathological Conferences.

A CONFERENCE AT SYDNEY HOSPITAL.

A CLINICO-PATHOLOGICAL CONFERENCE was held at Sydney Hospital on September 20, 1955, the medical superintendent, DR. NORMAN H. ROSE, in the chair. The principal speaker was DR. J. V. L. COLMAN, an honorary assistant surgeon of the hospital.

Clinical History.

The following clinical history was presented.

A hairdresser, aged fifty-seven years, was admitted to hospital complaining of yellow discoloration and itchiness of the skin. Off and on for twelve years he had had indigestion, with belching, the passing of flatus, "a lump in the throat, burning in the chest and coating of the eyes". He described these symptoms as occurring intermittently, with two or three weeks of freedom between attacks. He suffered no actual pain. For the last three months his stools had been white, his urine very dark, and his skin yellow and itchy, especially when he was warm. These features had been constant. He had lost two stone in weight, and vomited frequently, and his appetite had been poor. There had been no pain. He became slightly breathless on exertion and had a cough with some sputum. He smoked but did not drink alcohol. One sister had had obstructive jaundice, but no other members of his family had had relevant illnesses, nor was his own past history noteworthy.

On examination he was found to be thin and jaundiced. The epigastrium was tender, and an enlarged liver extended three fingers' breadth below the margin of the ribs. There was some guarding but no rigidity, ascites or masses. No abnormalities were found on examination of the chest, heart or nervous system. The blood pressure was 140 millimetres of mercury, systolic, and 80 millimetres, diastolic. There were no blemishes on the skin, no lymph gland masses and no fever. A test of the urine yielded a positive result for bile salts but not for albumin or sugar.

The results of special investigations were as follows. Blood examination showed a hæmoglobin value of 9·7 grammes per 100 millilitres; some anisocytosis and polychromasia were present, with a shift to the left in white cells, and some toxic changes; platelets were plentiful. The serum bilirubin content was 10·3 milligrammes per 100 millilitres. The prothrombin index was 84%. Excess urobilinogen was present in the urine. X-ray appearances of the chest were normal.

The provisional diagnosis was "malignancy". The findings at laparotomy will be revealed later.

Clinical Discussion.

DR. J. V. L. COLMAN: Clinical diagnosis will always depend first and foremost on the history and clinical examination, and secondly on the results of laboratory and radiological investigations, which should always be correlated with clinical findings. *In attacking the problem of the diagnosis* of jaundice the history and physical examination are of greater importance than liver function tests, and, as you can see, these tests do not offer much help in the case we are discussing today. No case of jaundice requires immediate surgery; so there is always adequate time for diagnosis and repeated observations to be made, and medical and surgical types of jaundice can be differentiated. I thought it would be a good idea initially, for the benefit of students present, to run briefly through the metabolism of bile pigments and salts.

As you know, red cells are constantly being destroyed in the reticulo-endothelial system, and hæmoglobin is liberated. Hæmoglobin becomes divided up into two parts—an iron-containing portion, which has a separate pathway of conservation, and bilirubin. Bilirubin is present in the plasma in combination with globin and cannot be excreted by the kidney; it produces an indirect Van den Bergh reaction. It passes to the liver, and the liver cells take it up, split off the globin and excrete it into the bile, in which it passes down the biliary passages to the duodenum. Then in the gut, by the action of bacteria, bilirubin is converted into urobilinogen. This bilirubin which leaves the liver cells gives a direct Van den Bergh reaction and can be excreted by the kidney. Urobilinogen in the intestine is for the most part excreted in the fæces, but some is reabsorbed into the portal circulation and passes to the liver where it is reexcreted. Some reaches the general circulation and is excreted in the urine. The urobilinogen of the fæces amounts to some 100 to 200 milligrammes per day and in the urine 0·5 to 1·5 milligrammes per day. Bile salts are manufactured in the liver and excreted into the bile. In the small intestine they carry on their metabolic activities and are for the most part reabsorbed and reexcreted. They do not normally appear in the urine.

There are three main varieties of jaundice—namely, hæmolytic jaundice, hepatic jaundice, both toxic and infective, and obstructive jaundice. In hæmolytic jaundice, owing to excessive destruction of red cells, an excess of bilirubin reaches the liver cells, which, although working at maximum capacity, are unable to excrete into the bile all the bilirubin which is combined with globin and which, therefore, cannot be excreted by the kidney. An obstructive element can supervene in hæmolytic jaundice, owing to the formation of bile thrombi in the canaliculi and pigment calculi in the common bile duct. Jaundice of the hæmolytic variety is usually not of severe intensity, and the colour of the skin rarely more than a light yellow. There is no pruritus, the stools are not pale, the serum bilirubin content does not exceed about 5·0 milligrammes *per centum* in most cases, and the Van den Bergh reaction is indirect. In the urine there are no bile pigments and no bile salts. Excess of urobilinogen is present in the urine and fæces. Hæmolytic jaundice is usually associated with anæmia, reticulocytosis and, in some cases, microspherocytosis, with increased red cell fragility, splenomegaly and a familial incidence. Hæmolytic jaundice may be symptomatic or secondary, as in septicæmia, malaria, pernicious anæmia, *icterus neonatorum* and erythroblastosis of the newborn. A second variety is congenital acholuric jaundice, a well-known syndrome. A third variety is the acquired hæmolytic jaundice in which there is an abnormal hæmolysin present in the plasma. Finally there is a fourth type, not particularly well known, which was brought to my notice by Dr. Johnston—chronic intermittent juvenile jaundice, about which I will say something later on.

Hepatic jaundice accounts for a large proportion of cases with medical jaundice, both toxic and infective. In this condition the liver cells are unable to cope with the normal amounts of bilirubin passing to them, and therefore there is an accumulation of bilirubin in the plasma. At the same time there also occur associated œdema and stasis in the biliary passages, with a resulting superadded obstructive element. The jaundice here is usually of moderate intensity and varies from a dark yellow to an orange tint. Pruritus may be present, but is never intense. The stools are never completely colourless. Bile salts and pigments appear in the urine, and urobilinogen is usually present in excess in the urine and fæces. Van den Bergh's reaction is biphasic, and the serum bilirubin content may reach a level of 20 or 25 milligrammes *per centum*. To distinguish this type of jaundice from that due to obstruction is often difficult in the first two weeks of the illness, but jaundice is never as intense, nor does it persist for as long as in obstructive conditions. The common infective hepatitis provides an example of this type of jaundice, occurring sporadically or in epidemics and associated with pyrexia, malaise, upper abdominal discomfort and tender liver. It presents like obstructive jaundice, but the jaundice usually begins to fade within a week and rarely persists for longer than one month. Other types of hepatic jaundice are caused by chemicals like phosphorus, arsenic and chloroform, and the jaundice associated with hepatic necrosis, carcinoma of the liver and chronic hepatitis.

The last type of jaundice is obstructive jaundice. Here bilirubin passes to the liver cells, is altered and is excreted into the biliary passages, where, owing to obstruction, it is reabsorbed. At the same time bile salts accumulate in the blood-stream. Jaundice is usually intense, and the skin may even be green in colour. The stools are pale, the urine is dark, and pruritus is a common feature, being due to an excess of bile salts in the blood-stream, often leading to scratching of the skin and perhaps furunculosis and shininess of the nails. Urobilinogen is absent from the fæces, which may be bulky owing to the presence of excess fat. Pancreatic enzymes are able to break down the neutral fats into fatty acids and glycerol, but the absence of bile salts prevents their absorption. The urine is dark because of the presence of bile pigments. Bile salts are present in urine but not urobilinogen. The Van den Bergh reaction is immediate and direct.

This afternoon we are presented with a case of obstructive jaundice of some three months' duration, which had been painless and constant. I should like to comment on a few points of history and the physical examination. First of all,

the patient was a hairdresser; but I know of no chemical agent to which he might have been exposed and which might have caused his illness. There was no history of alcoholism or of gastro-intestinal bleeding, no splenomegaly, no ascites and no skin blemishes such as spider nævi or dilated veins—which excludes a diagnosis of cirrhosis of the liver. As there was no familial tendency we exclude congenital acholuric jaundice, which is of the hæmolytic variety, and another type of hæmolytic jaundice, namely, chronic intermittent juvenile jaundice. This last condition was described by Meulengracht, of Copenhagen, in *The Quarterly Journal of Medicine* in 1937. It is a syndrome associated with slight jaundice and lassitude occurring at intervals. It is benign, becomes less intense and must not be confused with the more severe subacute and chronic forms of hepatitis. It has a familial tendency. In all other respects these patients are healthy. The jaundic fluctuates, but never gives more than a yellow tinge to the scleræ and skin, and in some cases only bilirubinæmia can be detected. It is a hæmolytic jaundice, and no bile pigments appear in the urine. No other abnormalities can be found in these people, though some fatty infiltration was shown in liver biopsy specimens from a few of the patients. According to the author, "predisposing factors are alcohol, convivial evenings, lack of sleep, sorrow, anxiety and overwork". I believe the obstructive jaundice occurring in the patient's sister indicates no familial tendency.

As regards the jaundice in this patient we do not know the intensity of colour of the skin and scleræ. We do not know whether it was progressive, or whether there had been any remissions, though we are told it had been constant. Examination of the urine showed the presence of bile salts, presumably determined by Hay's test, but no test for bile pigments was carried out. Bile pigments in the urine are most readily demonstrated by the foam test, in which the froth on the surface of shaken urine is coloured yellow, or by the iodine test. This is important in investigation, and the urine should be examined frequently to estimate the progress of jaundice. There is no record of a rectal examination having been carried out. The colour of the fæces should be observed at regular intervals. The liver was enlarged and tender, and this is a common finding in obstructive jaundice of long standing. We do not know the consistency of the liver and whether any nodules could be palpated. An enlarged liver is due to distension of the bile channels behind the obstruction and to extravasation of bile from the canaliculi. It is also associated with some central lobular œdema and necrosis of the liver cells, and later there may be a lymphocytic infiltration. Another feature is anorexia and loss of weight. This is common in all types of obstructive jaundice, whether due to malignant disease or to stone in the common bile duct. The blood count showed anæmia, with evidence of red cell regeneration, and probably leucocytosis, with a shift to the left and toxic changes in the white cells.

As regards the liver function tests, it must always be remembered that normally only about 25% of liver tissue is being utilized at any one time, and therefore the results of liver function tests may remain normal till the degree of liver damage is advanced. It is necessary to choose tests which do not overlap in measuring specific function, and these liver function tests are often of more use in indicating progress and the degree of liver damage than in making the diagnosis. The serum bilirubin content normally is less than 0·1 milligramme per 100 millilitres. Here it was 10·3 milligrammes per 100 millilitres. The measurement of serum bilirubin is probably of most value in detecting subclinical jaundice, in estimating the intensity of jaundice and in assessing progress from day to day. The Van den Bergh reaction appears satisfactory on paper, but it is not always reliable. In this case the reaction was immediate and direct. A direct reaction is given by post-hepatic bilirubin in pure obstructive jaundice, and an indirect reaction is produced in hæmolytic jaundice owing to the presence of pre-hepatic bilirubin which is combined with globin. In the indirect reaction, only after an interval or after the addition of alcohol does the bluish-violet colour develop with Ehrlich's diazo reagent. Some of the fallacies of the Van den Bergh reaction occur in all three types of jaundice. In hepatic jaundice, for example, where there is liver cell damage and therefore a delayed indirect reaction occurs, there is also superadded obstruction from œdema and stasis in the small bile channels, and a direct reaction may occur as well, giving a biphasic reaction. In hæmolytic jaundice there is an indirect reaction, but some obstruction may also occur, and again a biphasic reaction is found. In obstructive jaundice there is a direct reaction initially, but the liver cells may later be damaged, and a biphasic reaction will then occur.

The detection of urobilinogen is important. In order for it to be present in the urine and fæces, bilirubin must have entered the alimentary tract; and therefore if it is detected, obstruction cannot have been complete and constant. If urobilinogen in the urine comes and goes, then obstruction must be incomplete, as, for example, with stone in the common bile duct. These tests for urobilinogen should be done every day, for it is then that they are of greatest value. Estimates of total serum protein content and of the albumin-globulin ratio can be of value in estimating the degree of damage to the liver cell. Qualitative changes in the serum albumin and globin can be estimated by tests which include cephalin flocculation and the thymol turbidity test, and a raised serum alkaline phosphatase content in the absence of bone disease indicates obstruction.

We are told here that the prothrombin index was 84%. The coagulation time is increased and a tendency to bleeding occurs in hepatic jaundice owing to the inadequate formation of prothrombin by the damaged liver cells and in obstructive jaundice owing to inadequate absorption of vitamin *K* due to lack of bile salts in the intestine. A more helpful test would have been to give the patient vitamin *K* parenterally; if the prothrombin content rose, this would be evidence of obstruction, whereas if no change in the prothrombin index occurred, it would indicate liver cell damage. In most cases the serum alkaline phosphatase content (which is normally 3 to 13 units) and the thymol turbidity (normally 0 to 4 units) are of the greatest help in differentiating obstructive jaundice from jaundice due to liver cell damage.

The X-ray appearance of the chest was normal. Other radiological investigations might have included a barium meal examination to exclude any lesion or deformity of the stomach or duodenum. Cholecystography is contra-indicated in obstructive jaundice because the di-tetra-iodo-phenolphthalein used may precipitate acute pancreatic œdema; or because of the inability of the liver cells to excrete the dye, severe toxic symptoms may occur.

Obstructive jaundice arises when there is interference with the flow of bile in the biliary tract at any level from the bile canaliculi to the ampulla of Vater and may be due to intraluminal or extraluminal causes arising within or outside the liver. The causes are usually classified as: those within the ducts—namely, gall-stones, inspissated bile or parasites such as the liver fluke or ascaris—or causes in the wall of the duct or outside the duct. In the wall there may be sticture (congenital or acquired), carcinoma, catarrh of the duct (especially in the region of the ampulla of Vater associated with duodenitis) or pancreatic œdema. Causes of compression of the duct from outside include: carcinoma of the head of the pancreas and carcinoma of the ampulla of Vater; enlarged lymph nodes in the *porta hepatis* due to secondary carcinoma, lymphadenoma, leuchæmia, lymphosarcoma and secondary syphilis; tumours of the liver, both primary and secondary, and tumours of neighbouring organs (stomach, colon, right kidney and right suprarenal); and lastly hydatid cyst. The commonest causes of obstructive jaundice are stone impacted in the common bile duct and malignant obstruction of the biliary passages.

I should like to discuss some of the features which might help in differentiating these two conditions. A stone in the common bile duct producing obstruction usually impacts in the lower end and classically gives rise to what was described by Charcot in his triad of intermittent pain, intermittent fever and intermittent jaundice. Jaundice due to malignant obstruction has been described as being painless and progressive, but pain is often present and in some cases the intensity of jaundice varies. In obstruction due to stone, pain is absent in only a very small percentage of cases. In the vast majority it occurs as biliary colic, but it may occur as a less severe epigastric or lumbar pain or even as mild gall-bladder dyspepsia. In malignant obstruction, pain is usually described as being absent, but this is not so, especially in the early stages of the disease, when pain may be rather vague, periumbilical or epigastric and radiating through to the back or to the left shoulder. Rarely does severe colic occur. Fever occurs in about one-third of cases of obstructive jaundice due to stone and usually consists of a rise in temperature up to 100° to 103° F. associated with a feeling of chill, and this may be present in the absence of associated cholangitis. In malignant obstruction of the bile passages it is quite common for the temperature to be elevated intermittently, and therefore fever does not help very greatly in the differential diagnosis. The patient presented today had no fever. Jaundice due to obstruction by stone is described as being intermittent owing to the ball-valve action of the stone and to associated œdema, which may fluctuate. Jaundice is often more intense when a

single stone blocks the common bile duct than when multiple stones are present. The jaundice associated with malignant disease is progressive, but remissions can occur, being either due to variation in associated œdema or due to softening of the tumour or to sloughing of portion of the tumour.

A helpful sign in differential diagnosis is the detection of a palpable gall-bladder. According to Courvoisier's law, when a gall-stone impacts in the common bile duct the gall-bladder is impalpable in 80% of cases, owing to the fact that the gall-bladder has been the seat of previous infection and fibrosis then prevents distension. It may become palpable if the stone is a pigment stone arising in the duct or if it is a cholesterol stone which has arisen in a gall-bladder the seat of cholesterosis; in this condition the gall-bladder is still capable of dilating. The gall-bladder may also be palpable when a stone impacts in the common bile duct causing obstructive jaundice and there is associated obstruction of the cystic duct with the production of a mucocele or empyema. In malignant obstruction of the common bile duct, the gall-bladder is palpable in the large majority of cases, though it may not be palpable when the obstruction lies above the junction of the cystic and common bile ducts or when there has been previous gall-bladder disease resulting in fibrosis of the gall-bladder wall. In jaundice due to impaction of a stone in the common bile duct, the serum bilirubin content rarely exceeds 10 milligrammes per 100 millilitres, and jaundice is therefore of a less intense variety. In malignant obstruction the serum bilirubin content may rise as high as 50 milligrammes per 100 millilitres. As regards the stools, in obstruction due to stone they are usually pale for only a few days at a time; whereas in malignant obstruction they are always pale, unless the carcinoma is of the ulcerative type at the ampulla of Vater. Fæcal and urinary urobilinogen contents vary in cases of stone impaction when obstruction is intermittent; whereas in malignant obstruction both fæcal and urinary urobilinogen are always at a low level or may be absent from the urine and fæces.

The case today presents with obstructive jaundice in a man aged fifty-seven years. The jaundice is painless, constant and probably progressive, and I suggest that it is due to malignant obstruction of the biliary passages. Although the history of the preceding twelve years could be described as gall-bladder dyspepsia, there is not enough evidence in the history and physical examination to support the diagnosis of a stone impacted in the common bile duct. As regards the exact site and pathology of the malignant lesion causing obstruction, I cannot exclude carcinoma of the head of the pancreas; although in the vast majority of cases the gall-bladder is palpable, and vomiting is not a common feature until late, unless the stomach or duodenum is invaded or involved by pressure. I should like to suggest that the early symptoms, even though of long duration, do not exclude a diagnosis of gastric carcinoma which has caused jaundice by obstructing the bile ducts above the junction of the cystic and common hepatic ducts by enlarged metastatic lymph nodes in the *porta hepatis* or by direct invasion of the duct or by secondary deposits in the liver in the region of the *porta hepatis*. Frequent vomiting and the blood picture support this diagnosis.

When the diagnosis of jaundice due to malignant obstruction is made, the precise site of the obstruction and the underlying pathology are often obscure till the exciting moment when the abdomen is explored at laparotomy. This moment will arise shortly when Dr. Palmer tells us the results of laparotomy.

DR. ROSE: Dr. Colman has been into this most deeply and wonders whether in the interests of the patient any of the many and complex tests he has mentioned should have been carried out. On the other hand, should laparotomy be carried out earlier in many of our cases of jaundice in the medical wards? What is your experience, Dr. Calov?

DR. W. L. CALOV: I do not think there is any way of making the diagnosis in a case like this without operation. I should like to compliment Dr. Colman on his learned discussion. It has been very interesting, and he has done it very thoroughly and well. It should be of great value to the students who are here. No one can tell what this man had without opening him up and looking: that is how I feel about it. But I doubt whether it is certain that the gall-bladder was not palpable. The liver was said to be enlarged, but the mass which was palpated might easily have been the gall-bladder and not the liver at all. His early symptoms—lump in the throat, burning in the chest and coating of the eyes, which I do not understand—do not seem to me to be very much like those of gall-bladder disease, though I admit you can get almost any symptom in carcinoma of the head of the pancreas. On the other hand, a striking feature of the story is the implication that the patient survived. Whether he died later on is not related, but he survived the period in hospital; so it may well be that he did not have any extensive malignant disease. It could have been some simple thing causing complete obstruction, and then the loss of weight and so on would be caused by the liver failure.

DR. ROSE: It is most unusual for these meetings that the patient did not die.

DR. T. I. ROBERTSON: I think the importance of this particular type of problem is the separation of jaundice due to parenchymatous liver damage from jaundice due to primarily obstructive disease—that is, the separation of medical from surgical cases rather than pin-pointing the actual lesion. This is extraordinarily important. In my opinion one really needs all routine liver function tests to make that separation, and I think the emphasis should always be on whether or not the patient needs an operation. By using the routine tests which Dr. Colman has discussed so ably I think the distinction can be made in a large number of cases; but if there is doubt, and providing the immediate act of operating is not going to kill the man, I think that exploration should be the final answer. Microscopic examination of the stools would have helped here. In pancreatic disease the very nature of the stool is often almost diagnostic. Simple examination of aspirated stomach contents will often suggest the presence of a gastric carcinoma without going to the trouble of a full test meal or barium meal examination. I incline to the diagnosis of cancer of the stomach. But I was badly misled recently in a patient who was shown at operation to have Hodgkin's disease solely affecting the liver and glands of the *porta hepatis* and presenting in very much this way. Hodgkin's disease is unlikely, but it can present in this fashion. I would agree that carcinoma of the stomach is most likely.

DR. H. M. WHYTE: With regard to laparotomy—it is not often that I have thoughts which are surgically inclined; in fact it is not often that I have any thoughts at all—I think that it is sometimes delayed too long in medical cases. I think that a great deal can be discovered without resorting to laparotomy, but in selected medical cases it can be invaluable. But from the surgical point of view, I also think that the surgeon is sometimes not adequately prepared to carry out the investigations which might be necessary during laparotomy. We have had instances recently in this hospital, and they are always cropping up from time to time, where laparotomy is performed, and still no obstruction is found. I should like to hear the surgeon's comments on this; but, to my mind, the duct has to be opened and probed in those cases, and, secondly, the radiological exploration should be undertaken—that is, radioopaque materials should be injected and pictures taken in the operating theatre in an attempt to demonstrate the blockage.

DR. J. SCHNEEWEISS: There are two brief points I would like to make. One is really in the form of a question to the radiologist, and that is whether there is any contraindication to the use of intravenous contrast media in jaundice; if not, one might well have made an intravenous cholecystogram in this man before operation. The other is a small suggestion—to have investigated pancreatic function, by estimating the serum amylase or urinary diastase content, may possibly have been of some value. Further to Dr. Robertson's suggestions, a barium meal examination, while perhaps not showing a gastric carcinoma, may have helped in diagnosing a lesion in the region of the pancreas.

DR. ROSE: I think Dr. Colman might answer these questions later on.

DR. E. HIRST: The laboratory worker as part of the team in investigation of jaundice often finds difficulty in interpreting the significance of his finding.

The first problem concerns hyperbilirubinæmia. This almost always indicates organic disease. As Dr. Colman has pointed out, it does not always do so. The condition of chronic intermittent juvenile jaundice (or constitutional hepatic insufficiency) occurs often enough to be worth bearing in mind. The laboratory findings are negative, with the exception of impairment of bilirubin excretion as manifested by the bilirubin excretion test; rarely, spherocytosis may be found. The second problem is that of obstructive jaundice. As Dr. Robertson has clearly indicated, the differentiation of medical from surgical jaundice is often readily made. Less frequently it may be extremely difficult.

In these cases where one considers the possibility of obstruction, a decision to perform liver biopsy is reluctantly made. The histological picture may appear to confirm the presence of obstruction. At operation no obstruction is found.

Absence of a dilated bile duct may only mean that the obstruction is high up or intrahepatic.

If with adequate examination no obtruction can be found, the possible explanation may lie in testosterone or in chlorpromazine jaundice, both of which may produce a picture indistinguishable from that produced by organic obstruction. In addition similar pictures have been reported in cholangiolytic hepatitis (Watson and Hofbauer) and in xanthomatous biliary cirrhosis (Thannhauser). In the latter, subcutaneous xanthoma is reported to be a constant finding, but I have no experience in these last two conditions.

DR. ROSE: Have you any comments, Dr. Walsh?

DR. R. J. WALSH: The thought occurred to me, as it did to Dr. Calov, that the fact of the patient not dying may be of significance. This would, perhaps, make a dagnosis of malignancy unlikely. I wondered whether hydatid was worth considering or, what is often overlooked and has been overlooked here in the past, amœbic abscess of the liver.

Pathology Report.

DR. A. A. PALMER gave the following pathology report and showed photographs of the specimen and microscopic slides:

Two specimens were received. One consisted of 11 centimetres of duodenum with five centimetres of stomach attached and a segment of pancreatic tissue measuring six by six by three centimetres. The ampulla of Vater was enlarged, measuring 2·2 centimetres in maximum diameter and raised one centimetre above the mucosa. There were two openings on the ampulla, one at the apex and another near the base. Section showed the ampulla occupied by soft white papillary newgrowth. The pancreatic duct led to the centre of the growth, and two dilated bile ducts were also found leading into the ampulla.

The second specimen was a lymph node measuring 0·8 centimetres in maximum extent.

Microscopic Examination.—The growth is a papillary carcinoma, and its structure suggests an origin from the ampulla, common bile duct or pancreatic duct. Parts of the growth are poorly differentiated. There is no evidence of carcinoma in the adjacent pancreatic tissue or the lymph node. The pancreas shows patches of autolysis, which appear to have occurred after removal, as there is no leucocytic infiltration. The pancreatic duct does not appear to have been completely obstructed, as there is little atrophy or fibrosis in the pancreas.

Diagnosis.

Carcinoma of the ampulla of Vater.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Section of Medicine and the Section of Pathology of the New South Wales Branch of the British Medical Association was held on July 12, 1955.

Atherosclerosis.

PROFESSOR F. R. MAGAREY read a paper entitled "The Pathogenesis of Atherosclerosis" (see page 1049).

DR. G. V. HALL read a paper entitled "A Clinician's Views on the Pathogenesis of Atherosclerosis" (see page 1053).

Discussion.

DR. W. J. MCCRISTAL said that in the eyes of the pathologist there was probably no more mistermed condition in medicine than the coronary episode, and there was much need for a better understanding between the pathologist and the clinician as to the implications underlying its mechanism in atheroma. The clinical impression and laboratory evidence were not necessarily inconsistent with necropsy findings as was commonly supposed. As an illustration, an intimal hæmorrhage might escape detection unless it was meticulously searched for, and yet might initiate ischæmia resulting in sudden death from ventricular fibrillation.

Dr. McCristal said that he had been disappointed to find, at the atherosclerosis meeting in Chicago in November, 1954, that the concept of thrombogenic atheroma was little, if at all, entertained, and he considered that Professor Magarey had been unduly modest in presenting his work along with that of his senior, Duguid, in that particular. Without labouring the question, there was more than a suggestion that the lipid and thrombogenic hypotheses for atherosclerosis were complementary. Dr. McCristal wondered whether either Dr. Hall or Professor Magarey would care to comment on the statement of a well-recognized American authority to the effect that allergic disease of the vessel wall was responsible for a percentage of deaths in the thirty to forty years age groups.

Dr. Hall, in reply, said that when the American authority spoke of fatal coronary occlusion from allergic disease of the vessel wall, it seemed that he was referring to a type of arteritis such as occurred in *polyarteritis nodosa*. It was a well-known fact that arteritis was the underlying pathological condition in some cases of coronary artery occlusion. It was Dr. Hall's impression, however, that it was a very rare cause. Yater had reported it in one only of his 600 odd cases of death from coronary artery occlusion in young men of the American Army.

DR. F. B. BYROM said that in the human subject atheroma was invariably present except in early childhood. Although its causation remained obscure there seemed no doubt, as Professor Magarey and Dr. Hall had pointed out, that the physical strain imposed on the vessel wall by the blood pressure was concerned, and Dr. Byrom suggested that it would be useful to try to assess the importance of that factor. In a given artery the strain on the wall was directly proportional to the mean pressure, to the diameter of the vessel and to the mean life span. He was not familiar with the literature on atheroma, and wished to ask whether the comparative pathologists had ever tried to correlate those three variables with the incidence of atheroma in different species. Serotonin (5 hydroxy-tryptamine), the vasoconstrictor agent liberated from blood platelets during clotting, had been recently synthesized, and it seemed not unlikely that some of the acute symptoms accompanying thrombosis of atheromatous arteries might be partly due to spasm caused by local liberation of serotonin. That might explain the occasional dramatic response to heparin.

Professor Magarey said that comparative pathology might help a little, and as an example, the cockatoo, which was known to live to a ripe old age—even exceeding the usual life span of the human—was reported to show atherosclerosis in its larger vessels, very similar to the human lesion.

Dr. Hall said that it was of great interest to hear at first hand of the synthesis of serotonin, the vasoconstrictor agent isolated from the blood platelets during clotting. It did seem very likely that that was the explanation of the dramatic relief of pain by heparin in some cases. Professor Best, when he was visiting Australia two years earlier, had said that he thought the action of heparin in promptly relieving pain in myocardial infarction was due to its vasodilator effect. Neutralization of the effects of serotonin might well be the explanation for the dramatic action of heparin in some cases.

DR. H. M. WHYTE said that he had two questions to ask. The first fell between the two speakers, being concerned with the relation between the clinical and the pathological aspects of atheroma. Morris reported that the incidence of deaths due to coronary disease had been increasing in London, and yet the degree of coronary atheroma found *post mortem* at the same time had been decreasing. Perhaps Dr. Hall would care to comment on that. The second question was for Professor Magarey. Natural thrombosis was well known to occur within the cavities of the heart, and yet atheroma did not develop in varicose veins. Dr. Whyte wondered whether atheroma ever developed there.

Dr. Hall, in reply, said that it was difficult to comment on the statement by Morris that deaths from coronary disease had been increasing in London, and yet the degree of coronary atheroma found at autopsy had at the time been decreasing. There appeared to be a general world-wide tendency for deaths from coronary disease to be increasing. Dr. Hall had not heard previously that the degree of coronary atheroma found at autopsy had been decreasing. It was possible if that view was correct that arterial spasm, which as Dr. Byrom had shown occurred in cerebral vessels, might also occur in coronary vessels, and that it might be playing an increasing role under conditions of stress in this modern age producing coronary occlusion.

Professor Magarey said that it was true that atheroma, as such, did not appear on the mural endocardium, although lipid degeneration could often be demonstrated in thrombi occurring on both the valve and the mural endocardium. Yellow lipoid plaques were common enough on the aortic leaflet of the mitral valve, especially on its ventricular

aspect; but it was not known what relationship, if any, those lesions bore to atherosclerosis. Professor Magarey did not know whether atherosclerosis was to be found in varicose veins or not, but lipoid-containing lesions in veins appeared frequently at certain sites, an example of which he had given during the reading of his paper.

DR. W. J. SIMMONDS asked whether raised mean arterial blood pressure, increased pulse pressure and increased twisting and shearing movements associated with arterial pulsation were equally liable to produce damage to the intima of the artery.

Professor Magarey said that he was unable to unravel that particular problem. All three elements mentioned by Dr. Simmonds were closely related to one another, and it was quite conceivable that they each contributed to the inevitable wear and tear of the vessel wall, which, as was postulated, predisposed to the pathogenesis of atherosclerosis.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal North Shore Hospital of Sydney, Crow's Nest, New South Wales, on April 21, 1955. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staffs of the hospital.

Chronic Relapsing Pancreatitis.

DR. I. A. BRODZIAK showed a woman, aged forty-three years, who had been first admitted to hospital in 1951 with a three-months history of severe abdominal pain, mainly in the left hypochondrium, and vomiting. A large mass was palpable in the left hypochondrium. The serum amylase content was greatly increased, and barium meal examination showed a "filling defect" of the stomach. Laparotomy revealed areas of fat necrosis and a large pseudopancreatic cyst, which was drained. Three months later the patient underwent *paracentesis abdominis* for ascites, and another month later the pseudocyst was again drained at laparotomy. At that time the serum amylase content, the urinary diastase content and the fæcal fat content were all increased. The glucose tolerance curve was of the diabetic type. Subsequently the patient had recurrences of pain and vomiting, mostly at the time of menstruation, and was treated with pethidine, to which she became addicted. She was readmitted to hospital for recurrences in March, 1953, and again in February, 1955, when she had severe pain and vomiting and tenderness in the left hypochondrium. The serum amylase content was increased. Graham's test showed no abnormality, but plain X-ray examination of the abdomen showed areas of calcification in the pancreas. The patient was observed to have periods of hallucinations and delusions. During her illness the results of Benedict's tests of the urine were negative, and blood counts were within normal limits, although there was a persistently raised erythrocyte sedimentation rate.

Pernicious Anæmia.

Dr. Brodziak then showed a man, aged sixty-one years, who had suffered from total alopecia for forty-four years. In 1952 he had noticed swelling under the eyes and swelling of the ankles, and his condition was diagnosed as myxœdema, but treatment with thyroid produced little benefit. In January, 1951, he experienced generalized weakness and tiredness, and was admitted to hospital for investigation. His skin was found to be pale, dry, smooth and hairless. Both ankle jerks were absent, as was vibration sense in the lower extremities, and the left plantar response was extensor. The tongue was smooth and normal. Rectal examination revealed a firm, hard prostate. The hæmoglobin value was 7·0 grammes *per centum*, the total erythrocyte count was 1,600,000 per cubic millimetre, and the mean corpuscular hæmoglobin was 44 micromicrogrammes. The average size of the erythrocytes was greater than normal, anisocytosis and poikilocytosis were marked, and polychromasia was present occasionally. Platelets numbered 114,000 per cubic millimetre. Occasional Howell-Jolly bodies were seen, and two megaloblasts were seen during the counting of 200 leucocytes. The total leucocyte count was 2800 per cubic millimetre. Examination of the gastric contents revealed histamine-fast achlorhydria. Marrow biopsy findings were consistent with megaloblastic anæmia. The radiological appearances of the pituitary fossa and the twenty-four hour output of 17-ketosteroids were within normal limits. Vitamin B_{12} therapy was instituted, and on the seventh day the reticulocyte count was 13·6%, the hæmoglobin value 11·1 grammes *per centum*, and the total erythrocyte count 3,070,000 per cubic millimetre. The patient was receiving 100 microgrammes of vitamin B_{12} every second day. The neurological findings remained unchanged.

Hæmochromatosis.

Dr. Brodziak's last patient, a man, aged thirty-five years, had noticed loss of libido and impotence in 1947, and in 1951 had been diagnosed as suffering from hæmochromatosis. In 1953, glycosuria, polyuria and polydipsia were noticed, and treatment with insulin was begun. In November, 1954, he was admitted to hospital with an intermittent dull ache in the upper part of the abdomen. His skin was then brownish-grey, dry and scaly. The liver was greatly enlarged and smooth. Testicular atrophy and glycosuria were present. The serum iron content was 243 microgrammes per 100 millilitres. The latent iron-binding capacity was nil. The total iron-binding capacity was 243 microgrammes per 100 millilitres, and random non-fasting blood sugar values were 314 and 240 milligrammes per 100 millilitres. Examination for liver function revealed a serum bilirubin content of 0·5 milligramme per 100 millilitres, thymol turbidity of 0·5 unit, a serum albumin content of 3·5 grammes *per centum*, a serum globulin content of 2·4 grammes *per centum*, and a prothrombin index of 92%. The blood urea content was 40 milligrammes per 100 millilitres. Chest X-ray examination and blood count revealed no abnormality. The diabetes was fairly well controlled with insulin and an iron-free diet. Since discharge from hospital the patient had returned weekly for venesection.

Insulin-Resistant Diabetes Mellitus.

DR. F. H. HALES WILSON showed a woman, aged fifty-two years, who since 1949 had suffered from *diabetes mellitus*, discovered after psychic trauma caused by the untimely death of her son. She had previously had rheumatoid arthritis for four years. Early in 1950 she developed diabetic acidosis, but her condition was controlled for some months with a 1700-Calorie diet and a daily dose of 20 units of protamine zinc insulin and 80 units of regular insulin. Late in 1950 the daily dose of regular insulin had to be increased to 1000 units, and by 1951 the requirements had risen to 1300 units daily. Frequent allergic eruptions were occurring. In January, 1952, in an endeavour to reduce her insulin requirements, continuous mild hypoglycæmia was produced with a dosage of 1200 units three times a day. Improvement followed, and the dose was gradually reduced to 700 units daily. Slight fundal changes consistent with diabetic retinopathy were then apparent. By March, 1953, her insulin requirements had fallen to 280 units daily, with an 1800-Calorie diet, but they rose again in 1954, and immediately before the present admission to hospital she was receiving 1820 units daily. A maximum dose of 25,000 units daily was reached in March, 1955, and at present her glycosuria was not fully controlled with 16,000 units daily. Great difficulty had been experienced in giving such large, painful and frequent doses, but special Commonwealth Serum Laboratories insulin (300 units per millilitre) was now being used, with the addition of procaine and hyaluronidase. It had been found on two occasions that 8000 units given intravenously in about twenty minutes produced mild hypoglycæmic symptoms and substantially reduced her requirements for some days; they gradually rose again.

Acquired Hæmolytic Anæmia as the First Sign of Disseminated Lupus Erythematosus.

Dr. Wilson also showed a woman, aged nineteen years, who had suffered from recurrent painful swelling of the left wrist joint between 1952 and 1954, when the right wrist and right ankle were similarly affected. She was also treated for "pleurisy" with sulphadiazine; during the treatment she had transient urticaria and subsequently became weak and breathless on exertion. When examined in February, 1954, she was very pale and had painless discrete enlargement of moderate degree of her superficial lymph nodes, as well as painful wrists, which were not swollen. Her hæmoglobin value was 5·5 grammes *per centum*, and the erythrocytes were macrocytic and spherical. The reticulocyte count was 12%, the serum bilirubin content was raised, and the result of a direct Coombs test was positive. Those findings were consistent with acquired hæmolytic anæmia, and as numerous investigations revealed no other cause, sulphonamides were suspected. She was treated with ACTH for four weeks and a transfusion with specially cross-typed blood. Great improvement was effected, and although the result of the Coombs test remained positive, she was subjectively well when discharged from hospital in March, 1954. She remained well, although mildly anæmic, until January, 1955, when the arthralgia recurred. On readmission to hospital she was found to be pale and febrile with arthralgia of the hips, shoulders and knees. The hæmoglobin value was nine grammes *per centum*, with spherocytosis, normal fragility, increased urinary urobilinogen content and normal serum bilirubin content. L.E. cells were found in the peripheral

blood on two occasions in abundance. The result of the blood Eagle flocculation test was positive (this was considered to be a biologically false positive result), and an electrophoretic pattern showed a suspicious increase in the γ globulin fraction. These findings were thought to be consistent with a diagnosis of disseminated *lupus erythematosus*, which could well explain her clinical picture, although at no stage had her skin, renal tract, cardio-vascular system or nervous system been implicated. A maintenance dose of 75 milligrammes of cortisone daily was found to be suitable, and the patient was again discharged from hospital in an asymptomatic condition. She was being closely watched for further development.

Hodgkin's Disease with Spinal Cord Involvement.

DR. F. A. E. LAWES showed a man, aged thirty-one years, who had been admitted to hospital in 1951 complaining of pain and stiffness in the neck and right shoulder and weakness of the right arm for the past six weeks. These symptoms, mild at first, became very severe, and a burning pain spread from the neck to the right shoulder, arm, forearm and hand, with tingling in the fingers. Enlarged lymph glands were felt on both sides of the neck. Biopsy examination of these showed the changes of Hodgkin's disease with numerous large Reed-Sternberg cells. Thirteen days after his admission to hospital he had spastic paralysis of his four limbs, intercostal muscles and diaphragm. Only the accessory muscles of respiration were in action, and he was placed in a respirator, pain being relieved with "Omnopon". He was treated by intravenous injections of nitrogen mustard, 0·1 milligramme per kilogram of body weight per day being given (four injections of six milligrammes each). On the sixth day after the beginning of the treatment he was removed from the respirator and returned to the ward. All symptoms gradually subsided. He was given a transfusion of one litre of blood, because his leucocyte count had fallen to 1600 per cubic millimetre. He was discharged from hospital, symptom-free, after a stay of five weeks. Ten weeks later the pain in the neck and shoulder recurred, but it responded completely to a course of deep X-ray therapy given by Dr. Harold Ham. In March, 1952, he complained of pain in the left shoulder after heavy work, and also of some giddiness. He had nerve deafness of the right ear, but no other abnormal neurological signs. A further course of X-ray therapy was given. In August, 1953, he complained of a sense of pressure near the right ear and on the right side of the head, but no abnormality was found, and a diagnosis of nervous tension was made. He then settled down. In July, 1954, he complained of pain in the right side of the neck and the right shoulder, which came only when he was cold and subsided when he became warm. It was never troublesome when he was working. A diagnosis was made of trapezius fibrositis, probably the result of deep X-ray therapy. Dr. Lawes said that at present the patient's only complaints were of deafness and a discharge from the right ear due to chronic suppuration. The X-ray appearances of his chest were normal.

Toxic Hepatitis.

Dr. Lawes also showed a man, aged fifty-two years, who had been admitted to hospital in April, 1954. During the past four years he had undergone electroconvulsive therapy on some thirty occasions for a recurring depressive state. On March 31 he had commenced treatment with chlorpromazine, given orally. About ten days after the beginning of this treatment he became nauseated and later febrile, and then began to vomit. He had joint pain, headache, rigors, loss of appetite and colicky abdominal pain. Treatment with chlorpromazine was suspended on April 12, the total dosage given being then 1·5 grammes, and he was admitted to hospital on April 19. He was then obviously jaundiced, and his temperature was 102·2° F. The liver was not palpable, but he had generalized abdominal tenderness, maximal in the right hypochondrium. His blood pressure was well below normal. His urine contained bile pigments, bile salts and an excess of urobilinogen. The first fæcal specimen examined after his admission to hospital was pale. He had leucocytosis of the order of 15,000 cells per cubic millimetre, some 50% of which were eosinophile cells. A variety of biochemical, serological and radiological tests were carried out, but all with negative results. Three days after the patient's admission to hospital his temperature had fallen to normal, slight subjective improvement had occurred, but the deep jaundice remained. On May 3, liver biopsy by needle aspiration was carried out, and a diagnosis of biliary obstruction was made. At laparotomy the gall-bladder was found to be normal and the common bile duct was not dilated. When the duct was opened there was only a moderate flow of bile. When a probe was passed towards the *porta hepatis* there appeared to be obstruction at the origin of the intrahepatic portion of the common bile duct. The duct was drained with a "T"-tube. Convalescence was practically uneventful. The quantity of bile which drained each day was within normal limits. Cholangiography nine days after operation showed that the gall-bladder and bile ducts filled well and appeared normal. The biliary drainage tubes were removed on May 26, and at that time the jaundice was lessening and the patient was beginning to feel much better. The eosinophile cell count had fallen to 5%. Improvement was steadily maintained, and when discharged from hospital on June 12 the patient had almost completely lost his jaundice and was feeling well. When last seen, on December 23, he appeared perfectly well. In the interim further shock treatment had been given.

The Nephrotic Syndrome Treated with Corticotrophin.

DR. DOUGLAS ANDERSON showed a male patient, aged thirty-three years, suffering from the nephrotic syndrome. The patient had first entered the hospital with anasarca in 1953. Treatment by intravenous infusion of "Dextran" gave him a little relief, but not enough. The administration of cortisone for two weeks brought about profuse diuresis, and his weight fell to normal. Moreover, his albuminuria became very much less—his urine, which at first coagulated on boiling, contained little albumin on his discharge from the hospital.

He remained well and at work as an electrician for exactly a year and then relapsed for no apparent reason. He was readmitted to hospital and given an infusion of fractionated serum albumin in a dose calculated to double his plasma albumin value; but apparently this albumin left the circulation almost immediately. Corticotrophin zinc acetate was then given in a dose of 20 units every other day. After twelve days diuresis set in and he became as well as before.

The remission of the disease lasted only five weeks on this occasion. Serious anasarca soon recurred with pleural effusion on both sides. An infusion of four litres of salt-free "Dextran" promoted a good diuresis. Treatment with corticotrophin zinc acetate was resumed also; a dose of 20 units every other day was given for twelve days. He became very well, but after four weeks his weight began to rise again and a further eight-day course of corticotrophin was given, producing a good diuresis and further remission. After a further four weeks, as his weight was rising, it was decided to give a further course of corticotrophin and to continue with maintenance dosage. Prompt diuresis occurred and he was still well and at work at the time of the meeting three months later, the corticotrophin being continued in a dose of 10 units every other day. This amount had been increased to 20 units for three doses when a rise in weight and heavy albuminuria recurred. The increase in dose was followed by diuresis and the disappearance of slight œdema.

Atrial Septal Defect.

DR. G. E. BAUER presented three patients suffering from atrial septal defect. One, a girl aged eighteen years, was completely asymptomatic, the condition having been discovered during a routine medical examination in December, 1954. The second patient, a girl, aged seventeen years, had had greyish cyanosis for one week after birth, recurrent bouts of pyrexia at the age of ten years, when a heart murmur was first mentioned, "subacute rheumatic fever" for eight weeks at the age of eleven years, and a short illness at the age of fourteen years, characterized by transient albuminuria, ankle œdema and purpuric rash. She was now fully employed and in no way incapacitated by her heart lesion. The third patient, a girl, aged nine years, was said to have had a heart murmur at the age of one month. At the age of two years she had had occasional blueness of the lips, discovered after strenuous exertion, but this had not been observed during the past few years. She had slight dyspnœa on severe exertion, but the condition was not progressive. She had suffered from exertional syncope on one or two occasions. Details of the findings on electrocardiography, fluoroscopic examination and cardiac catheterization were presented for the individual patients.

Hæmochromatosis and Heart Disease.

Dr. Bauer's other patient was a man, aged forty-seven years, who had been found to have a heart murmur some ten years previously, when he complained of dyspnœa on exertion. There was no history of acute rheumatic fever, but at the age of fourteen years he had suffered from muscular pain, and at the age of sixteen years had been rejected for military service on account of "tachycardia". For several years he had suffered from indigestion, epigastric discomfort and flatulence after big meals. He had lost some weight during the past few years, but was able to lead a practically normal life. On examination the patient was found to have dusky skin with slaty pigmentation, general

sparsity of body hair, enlarged lymphatic glands palpable in the inguinal and axillary regions, a liver enlarged to below the umbilicus, and a spleen palpable one finger's breadth below the left costal margin. Examination of the cardiovascular system revealed sinus rhythm with occasional premature contractions, a blood pressure of 130 millimetres of mercury, systolic, and 80 millimetres, diastolic, and no evidence of congestive cardiac failure. The apex beat was left ventricular in character and was situated in the fifth left intercostal space, four inches from the mid-line. A systolic thrill was palpable, and there was a loud first heart sound and a grade IV systolic murmur maximal at the apex. No diastolic murmur was heard, nor were there any aortic murmurs. Electrocardiography showed the presence of mitral *P* waves in left ventricular preponderance. Fluoroscopic examination showed marked systolic expansion of the left auricle and left ventricular enlargement. Liver function tests showed raised values for thymol turbidity and zinc flocculation. The result of the blood Lange test was positive. Liver biopsy in 1952 revealed a great excess of iron-containing pigment typical of hæmochromatosis. Serum iron studies performed at the Red Cross Blood Transfusion Service by Dr. R. Walsh showed a high serum iron level with full saturation. The results of glucose tolerance tests performed in 1952 and 1953 were within normal limits, but in April, 1954, the results were diabetic in character. More recent results were not so high, but still outside normal limits.

Units of Neurology and Neurosurgery.

The Units of Neurology and Neurosurgery presented a series of patients.

Cerebral Abscess.

A boy, aged three years, had struck his head (the right frontal region) on December 2, 1954. Consciousness was not lost, but later he vomited and became drowsy. On December 10 he was admitted to hospital for investigation. The significant physical findings on admission were a temperature of 100° F., neck stiffness, Kernig's sign, normal reflexes and, later on, papillœdema. Lumbar puncture showed a raised cerebro-spinal fluid pressure and an increased lymphocyte content; however, the fluid was found to be sterile on attempted culture, but there was a leucocytosis of 17,000 per cubic millimetre. For six days after admission to hospital he remained drowsy, and the original diagnosis of cerebral abscess became more obvious. Eventually a left parietal burr hole was made, and, when the dura was opened, pus escaped. A brain needle was inserted into the left parieto-occipital region and two and a half ounces of pus were aspirated. The operation was concluded with the injection of "Thorotrast", so that serial X-ray pictures could show his progress. Intensive antibiotic therapy was also commenced and he began to improve. From the pus obtained at operation hæmolytic *Staphylococcus aureus* was grown.

His progress was satisfactory, although it took some time for his fever to resolve. On February 11 a second craniotomy was performed, when granulation tissue and the wall of the abscess cavity were excised. The source of the abscess was not apparent, and for this reason he was examined in consultation by the honorary cardiologist, who could find no evidence of congenital heart disease and thought that the systolic murmur which was present was of innocent origin. On discharge from hospital he was having half a grain of "Dilantin" three times a day and one-quarter grain of phenobarbitone three times a day. Further progress was to be assessed in the neurology clinic.

Guillain-Barré Syndrome.

A man of sixty-nine years began to complain of severe headache during the middle of August, 1954, and within a few days his speech became slurred and he developed a left facial palsy. About one week later he began to suffer from paræsthesia and severe pains in both lower limbs, which also became very weak and unsteady. The pain interfered with his sleep, and he was restless, noisy and confused at night. Early in September he became severely dyspnœic and developed a productive cough. At the same time both hands became weak and clumsy, and he experienced "pins and needles" in both upper limbs. His headache lessened gradually, but weakness and paræsthesia in all four limbs became progressively more severe.

On admission to hospital on September 10, 1954, he was cyanosed and dyspnœic, and had moist râles scattered over both lung fields. The optic disks and fundi were normal, but the left pupil was slightly larger than the right. He had a lower motor neuron paralysis of the left side of the face. Tone was diminished in all four limbs. The feet were held in plantar flexion, and there was a complete paralysis of both lower limbs from the hips to the toes. The arms and hands were weak and clumsy. Cutaneous sensation was lost over both legs below the knees and over both forearms, and he was unable to appreciate passive movement in the fingers or toes. The calves and muscles of the lower part of the back were tender to the touch. Tendon reflexes were absent in both upper and lower limbs, and the plantar responses were flexor. The heart was moderately enlarged to the left and the blood pressure was 200 millimetres of mercury, systolic, and 110 millimetres, diastolic. The findings of a full blood count were normal, but the erythrocyte sedimentation rate was raised to 11 millimetres in one hour (normal two to six millimetres). The blood Wassermann reaction was negative. Microscopic examination of the urine showed 10 to 20 red blood cells per high-power field; the blood urea content was 47 milligrammes *per centum*; a twenty-four hour specimen of urine contained neither arsenic nor porphyrins. The X-ray appearances of the chest, skull and spine were normal. The sputum contained no organisms, and no malignant cells were found. The cerebro-spinal fluid was clear and under a pressure of 140 millimetres of fluid. It contained two lymphocytes per cubic millimetre, 175 milligrammes *per centum* of protein, increased globulin, 733 milligrammes *per centum* of chlorides, and 99 milligrammes *per centum* of sugar. The Wassermann reaction was negative. The Lange colloidal gold curve was represented by the figures 2455210000. The electroencephalogram showed general dysrhythmia suggestive of encephalopathy.

He was treated with galvanism to the left facial nerve, physiotherapy, and large doses of vitamin B_1 by injection. The left facial palsy disappeared within four weeks, and cough and dyspnœa cleared during the same period. Though both lower limbs became atrophic, power slowly returned, and he was now able to walk with the aid of toe-raising springs and a stick. Strength in the arms and hands also improved considerably, and muscular pains ceased, though considerable sensory impairment was still evident.

Left Temporal Subdural Hæmatoma without History of Head Injury.

A man, aged forty-nine years, while surfing on January 15, 1955, suddenly experienced a peculiar sensation "like water rushing" in the left side of his head, followed by a left frontal headache, which persisted, but did not interfere with his usual activities. On January 23 he developed a fever and muscular aches, which responded rapidly to a course of tetracycline. The headache, however, persisted, and on January 24 he became dysphasic, complained of clumsiness and numbness of the right hand, and noticed drooping of the right angle of the mouth. Those symptoms decreased gradually, though some hesitancy of speech and difficulty with mathematical calculations in the course of his work continued to worry him.

On admission to hospital on February 11 he still had obvious difficulty in selecting the right word during conversation, but could name objects and understand all that was said to him. While there was no definite papillœdema, the optic disk margins were blurred and the retinal veins appeared congested. He had an upper motor neuron type of facial weakness, and the protruded tongue deviated to the right. Rapid repetitive movements were clumsily performed with the right hand, but there was no definite weakness or spasticity. No sensory defect was found. The tendon reflexes were normal and equal, and both plantar responses were flexor. His blood pressure was 155 millimetres of mercury, systolic, and 110 millimetres, diastolic. Plain X-ray examination of the skull revealed that the pineal gland was shifted six millimetres to the right. An electroencephalogram showed a focus of abnormal wave forms with phase reversals in the left mid-temporal region. In the left carotid angiogram the anterior cerebral artery was displaced to the right side, and there was an area of avascularity between the brain and the inner table of the skull, measuring 1·2 centimetres. This picture was diagnostic of a subdural hæmatoma. The blood Wassermann reaction was negative.

On February 11, Dr. J. M. F. Grant made a burr-hole in the left temporal region under local anæsthesia, and evacuated some four ounces of dark fluid from the subdural space. The patient made a rapid recovery from all his symptoms, and had remained well and free from headache since.

Diphtheritic Polyneuritis.

A woman, aged thirty-two years, had noticed difficulty in walking for two months before admission to hospital, preceded by an acute pharyngeal infection. Subsequently she had developed a choking feeling in the throat, huskiness of the voice, and regurgitation of fluids through the nose.

On examination the patient's right pupil was found to be larger than the left, but both pupils reacted to light and accommodation. There were bilateral palatal palsy, adduction and weakness of the vocal cord, and a suggestion of wasting and fibrillation of the tongue. There were left foot-drop and wasting of the muscles of the anterior and lateral compartments of the left leg. Lumbar puncture revealed a clear fluid under normal pressure. Microscopic and biochemical examination of the cerebro-spinal fluid revealed no abnormality. A test dose of neostigmine given subcutaneously failed to produce any lessening of the symptoms. It was considered that the patient was probably suffering from post-diphtheritic polyneuritis. She was discharged to attend the out-patient department for further observation.

Chronic Progressive Peripheral Neuritis.

A woman, aged sixty-two years, complained of a feeling of progressive weakness of her legs during the last ten years. Deterioration had been more rapid in the last four years. Her legs felt numb from the knees down. She had a tendency to fall over backwards and suffered severe cramps in the legs.

On examination she was found to be intelligent and cooperative. There was generalized wasting of the legs, most marked from about the middle of the thigh downwards, and weakness in the same regions. There was loss of pain, light touch and temperature appreciation in the legs from the middle of the tibiæ down. Proprioception and kinæsthetic appreciation were slightly impaired, and vibration sense was absent from the legs. The deep tendon reflexes of the legs could be elicited only with reinforcements, and no plantar response could be obtained. The ulnar nerves were thickened and insensitive. The blood pressure was 185 millimetres of mercury, systolic, and 120 millimetres, diastolic; otherwise physical examination findings were normal, as were the results of various other special tests.

The patient was considered to be suffering from chronic progressive peripheral neuritis not definitely differentiated from leprosy. It was considered that there was a large hysterical overlay to her illness. She was to return to the neurology clinic, and biopsy of the ulnar nerve was proposed.

Focal Paget's Disease of the Skull.

A man, aged fifty-seven years, had presented with a history of periodic headaches for over twenty years. They occurred about once a week, usually beginning in the early morning and lasting several hours. The pain was mainly frontal and bilateral, and the accompanying nausea, blurring of vision, photophobia and teichopsia in the form of spots and stars suggested a migrainous ætiology. During the past two years drooping of the left upper eyelid had occurred with most of the attacks of headache, and during the same period he became aware of a swelling in the region of the left supraorbital ridge. The only abnormalities found on physical examination were left-sided ptosis and a hard swelling of the left supraorbital ridge, extending upwards for about three centimetres above the left eyebrow, and downwards into the superior wall of the left orbit. This swelling was smooth and not tender to pressure. Plain X-ray examination of the skull revealed patchy, ill-defined areas of increased density in the region of the left supraorbital ridge and extending medially into the left frontal sinus, involving also the anterior end of the floor of the anterior fossa. The electroencephalogram was normal. The blood Wassermann reaction was negative. The cerebro-spinal fluid was normal in all respects.

A clinical diagnosis of meningioma *en plaque* in the left frontal region was suggested, and a left carotid angiogram showed a vascular blush in the region of the hyperostosis, though there was no displacement of the cerebral vessels. A pneumoencephalogram revealed no displacement of the ventricles.

On July 10, 1953, Dr. J. M. F. Grant performed a left frontal craniotomy and removed the thickened part of the left frontal bone and part of the left superior orbital plate and lateral wall of the left frontal sinus. The *dura mater* was adherent to the left frontal bone, but no meningioma was found. The patient made an uneventful recovery, and some six months later the bone defect was repaired with a tantalum prosthesis. He had remained well since then and free from severe headache, excepting for one attack of mild cellulitis over the left frontal sinus, associated with an upper respiratory tract infection, in January, 1955.

The pathologist's report on the excised portion of the left frontal bone read: "These pieces of bone have a loose cancellous structure. There is an irregular arrangement of the lamellar systems with well-defined cement lines giving a mosaic pattern characteristic of Paget's disease of bone. The marrow space is filled with a delicate fibrous connective tissue, in which the thin-walled blood vessels run. There was no neoplastic tissue to be seen."

A radiological survey of the entire skeleton revealed no other evidence of Paget's disease of bone.

A man, aged forty-five years, was first examined in October, 1953, when he complained of throbbing frontal headaches for the preceding three years. They occurred almost every morning and continued for most of the day, and were not accompanied by nausea or visual disturbances, nor were they aggravated by coughing or straining. The headaches had progressively increased in severity, and were only partly relieved by analgesic powders.

No abnormality was found on full neurological examination, and the blood pressure was 120 millimetres of mercury, systolic, and 80 millimetres, diastolic. Plain X-ray examination of the skull revealed an irregular area of increased density surrounding rarefaction in the right frontal region, and just below this was an irregular oval area of translucency with loss of diploic markings, measuring about three by two and a half centimetres. The pineal gland was calcified and in a central position. The electroencephalogram was normal, but after "Metrazol" activation an asymmetry appeared in the frontal region, the right side being of lower amplitude. The blood Wassermann and Kahn reactions were negative. A right frontal meningioma *en plaque* was suspected; a right carotid angiogram revealed a capillary blush in the right upper frontal region near the area of bone erosion, and a branch of the external carotid artery passed towards that blush. There was no displacement of the cerebral vessels.

On February 19, 1954, Dr. J. M. F. Grant performed a right frontal craniotomy. The bone was considerably thickened, but the underlying meninges and frontal cortex were entirely normal. A small biopsy was taken from the bone and the bone flap was then autoclaved and replaced. The patient made an uneventful recovery, and on review in February, 1955, reported that he had remained free from all headache since the operation.

The biopsy report on the bone chips removed during the operation stated: "The chips are composed of unusually dense bone. No other abnormality seen." A recent radiological survey of the patient's skeleton revealed no other evidence of Paget's disease of bone.

Extradural Hæmatoma of the Posterior Fossa.

A man, aged twenty-two years, was involved in a motor accident. On examination he was found to have anterograde and retrograde amnesia, and complained of severe headache. A large hæmatoma of the right orbit was present with some proptosis. He also had marked pulse irregularity. Subsequently he was shown to have paralysis of the right inferior oblique muscle, papillœdema and cerebro-spinal fluid pressure of over 300 millimetres with xanthochromic fluid. An electrocardiogram showed multiple mixed extrasystoles. An electroencephalogram showed well-marked changes due to trauma, greatest in the posterior temporal and occipital regions on the left. In a carotid angiogram there was a slight suggestion of displacement of the left anterior cerebral artery to the right. In a skull X-ray film a fissure fracture of the occiput was seen to extend from the *foramen magnum* to the lambdoid suture on the left. Burr holes were made in the skull and a large extradural hæmatoma of the posterior fossa was revealed. Post-operative progress was satisfactory, the cerebro-spinal fluid pressure returning to normal and papillœdema subsiding to some extent. The diplopia was also becoming much less. He was to return to the neurology clinic and to have further investigation of the diplopia privately.

Repair of Large Frontal Defect with Tantalum Plate.

A woman, aged thirty-nine years, had had an aneurysm clipped at craniotomy in November, 1952. Osteomyelitis developed in the frontal bone, and it was excised in May, 1954. The defect was repaired in January, 1955, with tantalum cranioplasty. All the cranium was entirely healthy. The patient had a very satisfactory post-operative course and returned to normal living.

Sudden Hemiplegia due to Intracranial Hæmatoma.

A woman, aged fifty-eight years, had experienced sudden pain behind the right eye in January, 1955, with left-sided weakness and neck stiffness. Her blood pressure was 160 millimetres of mercury, systolic, and 95 millimetres, diastolic, on her admission to hospital. Carotid angiography revealed displacement of the vessels to the left indicating a space-occupying lesion in the right frontal region. A pneumoencephalogram revealed displacement of the right lateral

ventricle, in its frontal part, upwards and to the left by the space-occupying lesion. At craniotomy on February 4, 1955, blood clot was aspirated from the frontal lobe. No further clot was removed at second-stage craniotomy two weeks later. The post-operative course was very good, apart from delayed healing of the anterior part of the wound. The patient had excellent return of power in the left limbs.

Status Epilepticus.

The last patient in this group was a man who had been well until six months before admission to hospital on February 26, 1955, when he developed intermittent colicky pain, insomnia, change of personality and inability to concentrate. In February, 1955, he vomited and had epileptiform convulsions. The fits recurred frequently in spite of anticonvulsant therapy.

On admission to hospital he was almost comatose, with increased tendon reflexes. Plantar responses were flexor; there was no papilloedema, but generalized muscle switchings occurred, and ankle clonus was also present.

Lumbar puncture revealed clear cerebro-spinal fluid, under pressure of 80 millimetres of fluid, with a positive Queckenstedt response, normal protein, chloride and sugar content, 162 erythrocytes and 33 lymphocytes per cubic millimetre, and no organisms; the Wassermann and colloidal gold reactions were negative. An electroencephalogram revealed abnormality predominant on the right side, but skull X-ray examination, a right carotid arteriogram and a pneumoencephalogram revealed no abnormality.

In spite of the exhibition of "Dilantin", "Prominal" and "Mysoline" he continued to have fits, persisted in a generalized hypertonic state, and displayed continual degeneration in condition, with dehydration and bronchopneumonia superimposed. Although fits ceased on March 3, 1955, he degenerated further until March 9, when he showed some improvement, which continued, with improvement of the state of consciousness and relief from bronchopneumonia until he was discharged from hospital, well, on March 25, still taking "Dilantin" and "Prominal".

Early in his illness his urine had contained increased amounts of porphyrin and coproporphyrin, so that it was suggested he might have been suffering a crisis in the course of porphyria. During his convalescence the porphyrins disappeared. Abnormal amounts of lead and arsenic were not found in his urine. The urine had no abnormality in cellular content and no organisms.

Cardiac Investigation Clinic.

Two patients were presented from the Cardiac Investigation Clinic.

Tetralogy of Fallot.

A boy, aged five years, who had had cyanosis at birth, was short of breath on exertion. He could walk only about thirty yards before squatting down to rest. On examination of the boy there was obvious central cyanosis and clubbing of fingers and toes. An increased right ventricular pulsation could be felt in the left parasternal area. A grade 3 systolic murmur was maximal in the third left intercostal space, and the second heart sound at the pulmonary area was single and moderately loud. The electrocardiogram showed *P-pulmonale*, right axis deviation and right ventricular preponderance; and X-ray films showed the heart only slightly enlarged, a small main pulmonary artery and diminished vascular markings in the lungs. A diagnosis of the tetralogy of Fallot was made, and a Blalock operation was carried out in March, 1954.

The patient had now lost his cyanosis, had grown rapidly, could walk a mile in comfort and did not squat. On examination of the patient, only slight clubbing could be seen and there was a typical continuous murmur of patent ductus type, which could be heard on the left side of the chest.

Mitral Stenosis.

A woman, aged forty-two years, had been short of breath for two years and noticed palpitation on exertion or excitement. She was short of breath on climbing one flight of steps or walking up a small incline. On examination of the patient, the pulse was of small volume, the blood pressure was 115 millimetres of mercury, systolic, and 85 millimetres, diastolic; the cardiac impulse was tapping in character. At the mitral area the first heart sound was loud and abrupt, the opening snap was easily heard, and there was a rumbling diastolic murmur with a thrill throughout diastole. The electrocardiogram showed a bifid *P-mitrale*, and X-ray films showed a heart of normal size with slight enlargement of the left atrium. Mitral valvotomy was carried out in May, 1954. The patient was now virtually symptomless and could carry on all normal activities without dyspnœa. The auscultatory signs remained almost the same as before operation.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

QUACKERY.

[From the *Sydney Gazette*, January 16, 1838.][1]

THE amount of Quackery in this our good town of Sydney is perhaps greater than in any other place of the same magnitude. The impunity with which individuals palm themselves off on the public as qualified to practise in the medical profession is truly astonishing. Perhaps some of these worthies are not aware of the heavy penalty attached to individuals practising without a licence: in the event of death ensuing from their tampering with diseases they do not understand, they are liable to be brought to trial and tried for the capital offence. If the law were to exercise its influence in one or two cases it might deter others from continuing their imposition. What injury may not such men do? It is a fact for which we can vouch, that persons in this town style themselves doctors, surgeons &c., and dispense medicine who at the same time know nothing whatever of the Materia Medica or any other branch of the profession. Fathers of families and others should beware how they employ these impostors.

Correspondence.

UNWHOLESOME NEWSBILLS AND THE PUBLIC HEALTH.

SIR: I have been unhappy about the tone of the newsbills published and displayed in the streets of Sydney of recent months by certain newspapers. With increasing and, I think, undue frequency the matter selected to advertise the newspapers on these bills has been concerned with sexual offences and perversion and with crimes of violence, especially with those involving the illicit use of firearms. Such newsbills thus seem to be obscene publications, as that term is defined by law, and also, in the true sense of the word, pornographic.

The proprietors of the papers concerned are public companies of colossal wealth and vast organization, directed by citizens of the highest standing and employing some of the best of the country's journalistic talent. There is something very unbecoming, surely, in the spectacle of these great companies crying their rape and gooseflesh in the market place. Yet the fact is that nearly every day they are publishing these base and meretricious appeals to the immature mind, parading and spotlighting the most evil examples of human behaviour even before those who do not buy the paper. The publications in question make terribly familiar those things that society in common prudence treats with discretion. They are thus manure for human soil in which the seeds of vice or delinquency may be implanted. I consider them to be in this respect a hazard to the public health.

What is the remedy? I doubt if recourse to legal process would do much good. It could cause much ill will and, if successful, would only excise the lesion from the tongue of the Press without treating the grave underlying disease. I wonder if our professional, scientific and religious newspapers, with their keen ethical sense, would take the lead in forming in New South Wales a voluntary Press council, like that set up in England in 1953. One of the objects of that council is said to be to maintain the character of

[1] From the original in the Mitchell Library, Sydney.

the Press in accordance with the highest professional and commercial traditions.

Yours, etc.,

185 Macquarie Street, Sydney,
October 15, 1955.

DOUGLAS ANDERSON.

THE TREATMENT OF CANCER IN NEW SOUTH WALES.

SIR: Dr. Harold Ham's letter concerning the treatment of cancer in New South Wales, and publicity in the lay Press, draws attention to a state of affairs that has caused concern for some time. Having discussed with Dr. Ham on many occasions the question of radiotherapy for patients suffering from cancer of the lung, I believe that the moderate tone of his letter, if anything, understates the true position. I therefore would like to make the following comments:

1. It is my opinion, based on experience in England, that close cooperation between physician, surgeon and radiotherapist will give the best results in the management of bronchial carcinoma as a general problem. Statistics do not do justice to the real value of well-directed radiotherapy in this disease.

2. In Sydney consultation with the radiotherapist, in the presence of the patient, is often difficult or impossible. This is particularly so in an institution such as the Royal North Shore Hospital, where there is no radiotherapy department.

3. Where there are no radiotherapeutic facilities in a hospital, and therefore infrequent attendances by a radiotherapist, there is little opportunity for discussion of individual problems and for assessment of progress and results.

4. In general, I am of the opinion that patients suffering from bronchial carcinoma whom I have referred for radiotherapy in Sydney do far worse than similar patients I saw so treated in London six to seven years ago. Radiation sickness is greater, large areas of skin erythema can be observed frequently following treatment, post-irradiation fibrosis in the sound lung has been seen on two occasions to cause death, and occasionally treatment is continued despite gross deterioration of the patient or even when obvious manifestations of distant metastases occur.

My own limited experience, therefore, would support Dr. Ham's statements concerning the lack of ordinary humane comforts for patients undergoing treatment, the almost complete absence of public hospital beds, and the difficulties of adequately planning and supervising treatment. These factors are related to the general shortage of hospital beds and lack of finance and are problems separate from that of scientific equipment.

Observations in the last few years would suggest that bronchial carcinoma, if not actually increasing in New South Wales, is certainly being diagnosed and referred for treatment more commonly and at an earlier stage. This disease, in fact, is now a major social problem in this country as elsewhere. Like most other surgeons I recommend radiotherapy for bronchial carcinoma only for selected inoperable cases or when the general condition of the patient precludes operation. Although it may well be that certain cases of lung cancer might be treated better by radiotherapy alone, or in combination with surgery, I personally would be unwilling to give such a policy a trial without access to an adequate radiotherapy service. At the present time in Sydney, where so little else offers, one feels obliged to extend radical operation in advanced cases beyond reasonable limits—even to the point of surgical foolhardiness.

Even allowing for a low operability rate, difficulties in early diagnosis and difficulties in securing hospital beds, one feels that a city of the size and wealth of Sydney should be able to offer something better than can be offered at present to the patient with cancer of the lung. The recent disclosures concerning radiotherapy, and other matters, can only mean that Sydney, at best, is a second-rate medical centre.

Yours, etc.,

135 Macquarie Street, Sydney,
December 2, 1955.

IAN MONK.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 3, 1955.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	2(2)	4(2)	..	4(4)	..	..	..	10
Amœbiasis	..	1(1)	..	..	..	..	..	..	1
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	1(1)	..	..	..	..	..	..	1
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1(1)	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1(1)	22(18)	10(6)	1(1)	..	..	..	1	35
Diphtheria	2	..	1	..	7(6)	..	..	..	10
Dysentery (Bacillary)	..	2(2)	6(6)	1(1)	..	..	..	..	9
Encephalitis	..	1(1)	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	55(23)	177(134)	..	18(8)	6(2)	..	..	..	256
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1	2(2)	..	..	..	..	..	..	3
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1(1)	1(1)	1	8(6)	1(1)	..	..	..	12
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	140(108)	..	18(13)	1(1)	..	..	..	159
Salmonella Infection	..	..	..	1(1)	1(1)	..	..	..	2
Scarlet Fever	15(13)	20(13)	16(7)	7(4)	..	..	..	..	58
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	..	1(1)	..	..	..	..	2
Trachoma	..	..	..	..	336(1)	..	..	..	336
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	30(20)	15(8)	4(1)	7(7)	6(4)	4(1)	..	..	66
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	1(1)	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Australian Medical Board Proceedings.

TASMANIA.

THE following have been registered, pursuant to the provisions of the *Medical Act*, 1918, as duly qualified medical practitioners: MacIntyre, John Reid, M.B., Ch.B. (Glasgow), 1938, F.R.F.P.S. (Glasgow), 1949; MacIntyre, Violet, M.B., Ch.B. (St. Andrews), 1943, D.M.R.D. (London), 1950; Unger, Pia Michaela, M.B., B.S. (Sydney), 1952; Cecil, Kevin Howard, M.B., B.S. (Melbourne), 1955.

The following have been granted Special Licences for one year under the *Medical Act*, 1951: Svoboda, Dobroslav, M.D. (Prague); Wirtz, Joe William, M.D. (Leipzig), 1938.

Congresses.

CONFÉRENCE INTERNATIONALE DES MALADIES RHUMATISMALES.

THE Société Médicale d'Aix-les-Bains is organizing the third *Conférence Internationale des Maladies Rhumatismales* to be held during the last week in June, 1956. The conference will study abarticular rheumatism and problems of the surgery of rheumatism. All correspondence should be addressed to the Secretary, Conférence Internationale des Maladies Rhumatismales, Boîte Postale 51, Aix-les-Bains (Savoie), France.

Notice.

AUSTRALIAN FEDERATION OF MEDICAL WOMEN.

THE Honorary Secretary of the Australian Federation of Medical Women advises that the Regional Meeting of the Medical Women's International Association will be held in Manila, The Philippines, from January 28 to February 4, 1956. The subject matter for the scientific sessions will be maternal and child welfare. Interested members are asked to contact the Honorary Secretary of the Medical Women's Society in their own State.

Medical Appointments.

Dr. C. A. Finlayson has been appointed official visitor to the Parkside Mental Hospital, South Australia.

Dr. K. P. McKenna and Dr. C. G. Wilson have been appointed honorary clinical assistants to the surgical section, Royal Adelaide Hospital, South Australia.

Dr. N. D. Abbott has been appointed medical registrar at the Royal Adelaide Hospital, South Australia.

Dr. R. B. Holland has been appointed to the State Hospitals and Homes in the Department of Public Health, New South Wales.

Dr. H. H. Moy and Dr. B. F. C. Smith have been authorized to sign permissions and certificates for cremation, and to grant permission to cremate any human body after death, under the provisions of *The Cremation Acts*, 1913 *to* 1935, of Queensland.

Research.

OPHTHALMIC RESEARCH INSTITUTE OF AUSTRALIA.

ATTENTION is drawn to the existence of funds in the Ophthalmic Research Institute of Australia available for research in any branch of ophthalmology. Further particulars can be obtained from the Honorary Secretary, Dr. W. Deane-Butcher, 235 Macquarie Street, Sydney.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

McKessar, John Hubbard, M.B., B.S., 1954 (Univ. Sydney), Sydney Hospital, Sydney.

The undermentioned has been elected as a member of the South Australian Branch of the British Medical Association:

Bowering, Douglas Charles, graduated 1954.

Diary for the Month.

JAN. 3.—New South Wales Branch, B.M.A.: Council Quarterly.
JAN. 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JAN. 13.—Queensland Branch, B.M.A.: Council Meeting.
JAN. 13.—Tasmanian Branch, B.M.A.: Council Meeting.
JAN. 16.—Victorian Branch, B.M.A.: Finance Subcommittee.
JAN. 17.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JAN. 19.—Victorian Branch, B.M.A.: Executive of Branch Council.
JAN. 25.—Victorian Branch, B.M.A.: Branch Council.
JAN. 27.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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